Tetanus in Bundelkhand Region - its incidence and the role of intrathecal human antitetanus immunoglobulin in its treatment

THESIS

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C E R T I F I C A T E

This is to certify that Dr. RAJIV DAS has worked on the topic " TETANUS IN BUNDELKHAND REGION-ITS INCIDENCE AND THE ROLE OF INTRATHECAL HUMAN ANTITETANUS IMMUNOGLOBULIN IN ITS TREATMENT", under my guidance and supervision. His results and observations have been checked and verified by me from time to time.

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C E R T I F I C A T E

It is hereby certified that the work entitled " TETANUS IN BUNDELKHAND REGION- ITS INCIDENCE AND THE ROLE OF INTRATHECAL HUMAN ANTITETANUS IMMUNOGLOBULIN IN ITS TREATMENT", has been carried out by DR. RAJIV DAS himself in this department.

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A C K N O W L E D G E M E N T S

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INTRODUCTION

I N T R O D U C T I O N

Tetanus is an acute toxaemic illness caused by the fixation of a neuroexotoxin in the Central Nervous System (C.N.S.), elaborated by the slender, spore forming, gram positive, anaerobic bacillus 'Clostridium tetani'. The word tetanus is an adaptation of the Greek word 'tetanos' which is derived from the verb 'teino' which means to stretch. Tetanus was first described by Hippocrates in the year 460 B.C.

This disease has a global prevalence, a high mortality and continues to pose a challenge to medicine. In rural India tetanus is rated as one of the first five leading causes of death. It is an extremely painful and debilitating disease that can leave the patient in a depressed and exhausted state months after the main symptoms have passed away.

The bacillus Clostridium tetani was isolated by Nicolaier in 1884 and its exotoxin in 1890 by Kitasato. This terminal spore bearing rod shaped bacillus is an obligate anaerobe, which settles deep in dead and defenceless tissues to produce one of the most lethal infections known to man. The toxin reaches the C.N.S. and blocks in-

hibition of polysynaptic reflexes, resulting in the characteristic clinical features of this disease. Muscular rigidity persits throughout the illness, punctuated by paroxysms of painful spasms of the voluntary muscles like masseters (lock jaw), the facial muscles (risus sardonicus), the muscles of the back (opisthotonos), abdominal and lower limb muscles, as well as convulsions. The patient remains conscious throughout the illness being a silent spectator of his sufferings.

The annual mortality from tetanus all over the world is above 50,000 (Bianchi (1961), Bytchenko (1966)). However this disease is more common in tropical countries and developing nations. Tetanus is more common in places with a warm and moist climate. Over 50,000 cases are reported annually in India by Health authorities. Basu et al (1984) reported the prevalence of tetanus neonatorum all over the 14 states and Union territories of India, the highest mortality due to tetanus being in Uttar Pradesh.

Tetanus may manifest at any age and may be divided into neonatal tetanus, childhood tetanus and adult tetanus of which the neonatal type contributes to

the highest mortality due to this illness. Geographical, social, cultural and economic factors interrelate to form an important back-ground for the prevalence of this disease. Illiteracy, inadequate medical care, unhygienic obstetrical practices, lack of immunization and ignorance contribute to the high incidence and mortality due to this disease.

Respiratory failure is a very important problem in tetanus. Tetanic spasms narrow the upper airway, impede the mobility of the thorecic cage and abolish protective reflexes of coughing and swallowing. Infection and aspiration of gastric contents into the lungs are common sequelae. A ventilation to perfusion mismatch, further exacerbates hypoxia. Apnoeic spells of central origin occur in the severest form of tetanus to which drugs used to control spasms, unfortunately contribute. In contrast to the impaired delivery of oxygen to the tissue there exists an increased demand for oxygen and calories by persistently contracting muscles (Khanna S.S. et al).

The therapy of tetanus has been a subject of dispute. Too many regimes have thus resulted with only partial success and high mortality rates. Intermittent

positive pressure ventilation (I.P.P.V.) and curarisation, beta-blockers, tracheostomy, antibiotics, intravenous fluids and nutrition, morphine, parentral magnesium sulphate infusions, centrally acting muscle relaxants (e.g. methocarbamol), diazepam, phenobarbitone, phenothiazines, chlorpromazine, paraldehyde, have all been used as supportive therapy in tetanus, each having its own merits and demerits. A standard form of supportive therapy nowadays, is the use of parentral diazepam as sedative, methocarbamol as a centrally acting muscle relaxant, parentral antibiotics notably penicillin and parentral fluids and nutrition.

The mainstay of the treatment however lies in the specific therapy of tetanus with tetanus antitoxin. Initially only equine antitoxin in the form of Antitetanus Serum (A.T.S.) was available. This too had its own limitations. Firor (1946) and Kryzhanovsky (1971) demonstrated the superiority of intrathecal over intramuscular route of A.T.S. administration. Sanders et al, demonstrated the beneficial effects of A.T.S. in human beings.However allergic reactions, short half life and fear of damage to the central nervous system by the preservatives used in the equine antitoxin have discouraged its human use. Pratt went to the extent of suggesting

that intrathecal administration of A.T.S. should be stopped until a newer, safe, antitoxin without any side effects is discovered.

Fortunately now with the availability of human antitetanus immunoglobulin (T.I.G.) interest in intrathecal administration has been revived. Being a homo-logous protein unlike A.T.S. (equine), T.I.G. (human) doesnot carry the risk of sensitivity reactions including anaphylaxis. At present intramuscular, T.I.G. is still being used. However the intrathecal use of T.I.G. by some workers appears to show good results, although some have doubted its efficacy.

The theoretical basis for intrathecal administration of T.I.G. is that when given systemically the large molecules cannot cross the blood brain barrier and so cannot neutralise unfixed toxins already present in the C.N.S. (Ildirim et al). Furthermore nowadays human T.I.G. is available in purified form and in high concentrations without preservatives which could damage the C.N.S. So far only a few studies have been done on tetanus cases indicating or giving beneficial effects of the role of intrathecal T.I.G. This present study includes a study of this newer form of therapy in tetanus.

Preventing tetanus is much simpler, cheaper, easier and very effective as compared to its treatment. In the long run human health, happiness and useful longevity can be achieved at a far less expense with less suffering through primary prevention. But all this requires proper health education and management which is unfortunately lacking in the Bundelkhand region.

The Bundelkhand region comprises of five districts of Uttar Pradesh and six districts of Madhya Pradesh with a total population of over 800000 people. Though historically and culturally rich this region is a poverty stricken, illiterate and socio economically backward area thus contributing to a high incidence of tetanus in this region. Clearly there was a need to explore cheap and effective means of controlling tetanus when it had already struck the patient. Comparatively the use of I.P.P.V. and curarisation is cumbersome, expensive and requires the presence of highly skilled personnel. In rural hospitals this is not possible. Encouraging results with the use of intrathecal T.I.G. have in fact paved a new way in tetanus therapy. This would indeed be a milestone in achievement of the above goal.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Tetanus is an acute toxaemic illness resulting from the effect of soluble exotoxins of the bacterium Clostridium tetani on the C.N.S.

This disease has a world-wide prevalence and is known by different names in different countries. It is known as"Dhanurvata " (India),"Hausa" (Nigeria), "Mal de arco" (Maxico), "Disease of Seventh day" (Algeria), "Po-Shian-Fong" (China), (Bytchenko).

The approximate global incidence of tetanus is 350,000 cases with total deaths exceeding 160,000 per year (Adams et al, 1969).

Theaverage annual mortality rates per 10,000 inhabitants of the world range from 0.05 up to 32,00 (Bytchenko).

Mortality from tetanus rises towards the equator as compared to the polar regions, reaching its zenith in the tropical and subtropical regions, mainly in Maxico, Central America, Peru, Ecuador, Colombo, Venezuela, Guyana Paraguay, Brazil, Equatorial Africa, India and New Guinea (Athavale et al).

History

In ancient India Charak described Tetanus as " wind Disease ".

Hippocrates in 460 B.C. was among the first to described this disease and its poor prognosis.

Sir, Charles Bell in 1836 first described "Cephalic tetanus " a rare clinical variety of tetanus.

The bacillus " Clostridium tetani " was isolated by Nicolaier in 1884.

Kitasato (1889) established the relationship of Clostridium tetani with tetanus. Tetanus exotoxin was isolated in 1890.

Neural transport of tetanus toxin into the C.N.S. was first described by Marie and Morax (1902) and Meyer and Ransom (1903).

Wright et al (1951), Fedinec (1965) Habermann et al (1970) & Kryzhanovsky (1967) have in the recent times confirmed the theory of neural transport of tetanus toxin into the C.N.S. Tetanus antiserum was introduced into clinical medicine in 1890 by von Behring and Kitasato.

The antitoxin was introduced for human use by Ramon and Zoeller (1933).

Bouyer (1926) suggested that pregnant women can be immunized against tetanus to protect the neonates.

Incidence

Although tetanus is present all over the world it is more common in the tropical & subtropical countries. The average annual incidence of tetanus in India during the period 1973-1982 was approximately 46,000 cases in an average population of 648 million. The incidence rate was therefore 6.7 per lakh population. According to the bulletin of Central Bureau of Health Intelligence 1983, total number of deaths due to tetanus in India during 1973 was 4569 out of 37,867 cases and during 1983 it was 5177 out of 31,368 cases reported.

Tetanus Neonatorum

While tetanus can occur at any age, the newborn are at a greater risk, because of the unsatisfactory and unhygienic delivery practices and lack of maternal immunization. The alarming nature of the problem due to tetanus neonatorum can be assessed from the data available. In the underdeveloped nations neonatal tetanus may effect as much as 8% of all live births and account for 30% of all neonatal deaths (Forfar J.O. 1973). According to Stanfield et al, results of community based surveys show that neonatal tetanus mortality ranges from less than 5 to more than

60 per thousand live births; these deaths represent between 23% and 72% of all neonatal deaths. Bytchenko (1972) and Cook (1983) have reported, that about 5 to 10 lakh deaths due to tetanus occur all over the world yearly, of which about 50% are neonates. According to Stanfield et al (1984) it was estimated that approximately 5 lakh deaths from neonatal tetanus occur annually in the WHO South East Asia and Eastern Mediterranean region alone.

In rural India tetanus neonatorum is rated as the second commonest cause of neonatal mortality (Shah P.M. & Udani P.M.). According to sample surveys neonatal tetanus mortality rates in 1981 were estimated to the on an average, 13.3 per 1000 live births in the rural areas and 3.2 in the urban areas in India (Sokhey et al).

It was also estimated that 2.3 to 2.5 lakh infants died within the first month of life due to tetanus neonatorum during 1981 (Sokhey et al). Nearly two thirds of these deaths were in Uttar Pradesh.

That tetanus neonatorum prevails in all the 14 States and Union territories of India has been

reported to be higher in the rural areas as compared to their urban counterparts. Tetanus as a cause of neonatal death ranged from 0 to 68.7% in the urban areas and from 16.4 to 72.5% in the rural areas (Sokhey et al). According to Sharma et al, case fatality rate of tetanus neonatorum in rural areas was around 97% and 80% in the urban areas. That neonatal tetanus mortality is not uniform in the different states of India is indicated by the available data.

The neonatal tetanus mortality rate per thousand live births was found to be 66.7 in rural Uttar Pradesh, 15.3 in Urban Uttar Pradesh, 4.7 in rural Maharashtra 4.9 in urban Maharashtra, 8.4 in rural Haryana & 1 in Delhi according to a recent nation wide survey (Basu R.N., Sokhey J, 1982).

Neonatal tetanus mortality was found to be 20 per thousand live births in Madhya Pradesh. In the rural areas of Rajasthan and West Bengal the neonatal tetanus mortality rates were between 20 & 10 per 1000 live births (Sokhey et al). It was recorded as a cause in 1/3rd or more neonatal deaths in Bihar (rural/urban), Kerala (rural/urban) and Tamil Nadu (rural).

Tetanus in Children

This implies tetanus in children between the age of 1 month and 12 years. Athavale et al, observed

that the maximum number of cases in children (excluding neonates) were between 2 to 5 years of age and they constituted 39% of total cases in children.

74% of the cases in children resulted from injury and otorrhoea (Athavale et al).

Jolly et al, noted a mortality of 37.69% due to tetanus, in children.

Tetanus in Adults

This includes patients beyond 12 years of age. Jolly et al, observed that the maximum incidence of adult tetanus was in the age group of 21 to 30 years. It was 23%. The highest mortality due to tetanus in adults was observed in the age group of 41 to 50 years (76.47%). A very high incidence of tetanus has been noted in Punjab. It was 90.4 per 100,000 cases per year (Gordon et al). Injury has been noted as an etiological factor in most of the cases of adult tetanus (38%), while the cause of tetanus was unknown in a significantly large number of cases (35.5%), (Jolly et al).

Incidence and Mortality in relation to sex

A higher incidence of tetanus has been noted in males by many authors. Kacharevic was the first to suggest that males appear to be more sensitive to tetanus

toxin, than females. His postulation was substantiated, by his observations on experiments with pigs and other animals.

Denchev noted a similar observation. Modi (1965) also suggested a higher incidence and mortality due to tetanus in males, as compared to females in all age groups. Raju et al also noted a slight male predominance of tetanus.

However Suri, Newell and Martin Bouyer noted that mortality did not differ significantly in the 2 sexes.

Indira Bai et al (1975) noted a lower mortality rate in males (74%) as compared to females (88%).

Urban and Rural tetanus

Tetanus mortality has been reported to be higher in patients in rural areas as compared to their urban counterparts. According to Sokhey et al, mortality due to tetanus ranged from 0 to 68.7% in the urban areas and 16.4% to 72.5% in the rural areas. Stanfield et al, also noted a significant rural/urban difference in tetanus mortality. It was 67 per thousand live births in rural Uttar Pradesh, whereas it was 15 per thousand live births in urban Uttar Pradesh (Stanfield et al). In an urban

centre like Delhi the mortality was 1 (Basu et al, 1982).

A survey by the Registrar Generals Office in India revealed that tetanus accounted for 15.6% of deaths below 1 year of age in rural areas and 6.6% in urban areas (Sharma et al).

Incidence rates of neonatal tetanus are highest in rural areas, where births usually occur at home and are attended by untrained personnel. Mortality in untreated cases is probably greater than 90% (Sokal et al).

Seasonal Variation of tetanus

Some authors have reported a higher incidence of tetanus during the rainy season (Gupta et al, 1977). Bhat et al, noted that maximum number of cases of tetanus neonatorum were admitted during the monsoon season i.e. between June and October. He attributed this increased incidence to the greater risk of contamination and infection during this season.

However Vakil et al (1964) found no significant seasonal variation.

As regards mortality due to tetanus, Sanders et al, found a significantly reduced mortality during the

hot, humid months of August to October as compared with the cooler, dry months of November to February. One of the factors of decreased mortality during the humid season was the reduced incidence of bronchopneumonia and dehydration due to the humid season (Sanders et al).

Puerperal tetanus

Unhygienically and improperly performed deliveries, poor domiciliary practices, poor post partum care, unhygienically and improperly conducted illegal abortions result in increased incidence of infection and subsequently to a high incidence of post partum and post abortal tetanus.

According to the observations of Shrivastava and Chatterji (1961), Shah et al (1962) & Bhatt (1962) puerperal tetanus contributes 10 to 12.7% of all cases. Mortality rates due to puerperal tetanus varies from 49% to 100%.

Social factors

According to Sanders et al in a study conducted by him he found that tetanus had a high prevalence among the poverty stricken, undernourished, rural based individuals who were working as cultivators or agricultural labourers. Illiteracy was rampant in such a population and

they lived in a crowded atmosphere in close contact with cattle and pigs alike. He also noticed that the commonest tetanus tragedies were among potentially healthy, child bearing women who were deprived nutritionally when they needed it most. This was all due to the poor social customs.

In new Guinea, women during childbirth and puerpendium are considered unclean and are forced to live in Menstrual houses where no man can visit them. In India also the pregnant women goes to her parents house for delivery (Usually in a village). She is considered untouchable during the first 10 days. Naturally tetanus is more prevalent under such conditions. Jolly et al, noted an excessive prevalence of tetanus in Punjab. He attributed this to Punjab being predominantly an agricultural state and that there existed a very close contact between the animals and human population in the rural areas. Illiteracy, lack of immunisation and the vague belief that cowdung was the best antiseptic to be applied on the wounds, all contributed to a high incidence of this disease.

Tetanus neonatorum may be considered as one of the penalties of underdevelopment manifested by poverty, illiteracy, ignorance, dangerous rituals, unhygienic customs, superstitions, religious prejudices and inappropriate

medical care. The incidence of tetanus neonatorum varies inversely with the development of MCH and obstetrical services. In the developing countries midwifery is still practiced by untrained midwives or local elderly women. They are known as"dais" in India, 'dukun' in Indonesia and 'montamyae' in Thailand (Bytchenko 1966).

Newell et al (1966), reported that the highest rate of 35 tetanus cases per 100 births was observed in neonates deli-vered by a blind midwife in Gauchene, Columbia, South America.

Incubation period

Incubation period is defined as the time interval between the entry of the organism in the host and the appearance of the first symptoms. In tetanus neonato-rum the incubation period corresponds to the age of the baby in most cases (Athavale et al).

A shorter incubation period has been found to be associated with a greater mortality by most workers (Athavale et al; Jolly et al, Phatak et al, Bhandari et al, Beaty and Jaffari et al) especially if it is less than 7 days. Bhat et al noted a mortality of 100% in neonates in whom the incubation period was less than 5 days.

Period of onset

This denotes the time interval between the first symptom and the onset of first spasm. In newborn the

the first symptom is usually persistent crying or inability to suck. In children & adults it is usually trismus. The prognostic value of the period of onset was first noticed by Cole when he found that a shorter period of onset was associated with a worse prognosis. Similar observations have been noted by Athavale et al, Jolly et al, Bhat et al, Phatak et al, Bhandari et al, Armitage et al(1978) & Patel et al.

Increased neuromuscular irritability

In tetanus patients increased neuromuscular irritability manifests in the form of generalised rigidity and spasms. The generalised rigidity is because of the increased muscle tone. This persists throughout the illness and is not affected by sedatives. Spasms (convulsions) are spasmodic contractions of muscles which may be tonic or clonic (usually tonic), which it self limiting and can be controlled by sedatives. Increased neuromuscular irritability of the facial muscles results in Risus sardonicus and that of masseters in lock jaw.

Grading of severity in tetanus

This is done on the basis of the criteria laid down by Patel and Joag (1959). According to this system a tetanus patient may present with any or all of the following five criteria.

Criterion No. I:- Presence of lockjaw/inability to suck.

" II:- Presence of spasms.

" III:- Incubation period of 7 days or less.

" IV:- Period of onset - 48 hours or less.

" V:- Fever on admission i.e. Axillary temperature of 99° F or Rectal temperature of 100°F on admission or within 24 hours of admission.

The cases having one of the five criteria are termed as grade I, the cases having only two of the five criteria, as grade II, cases having all the five criteria as grade V and so on.

Differential Diagnosis

Diagnosis of tetanus is usually straight forward and is based on the characteristic clinical features of this disease namely, risus sardonicus, lockjaw, generalised/localised rigidity, opisthotones, neck rigidity, dysphagia, reflex spasms, spasms (convulsions).

However there are certain conditions from which it has to be distinguished:

a) Meningitis

Trismus is usually absent in meningitis. There is high fever alongwith signs of meningeal irritation (positive leg raising test etc.). WBC counts and C.S.F. examination are diagnostic.

b) Epilepsy

In epilepsy the patient may lose consciousness which may be even momentary, whereas a tetanus patient remains conscious throughout the illness. The patient may also give a previous history of similar seizures with completely symptomfree intervals.

c) Strychnine poisoning

This results by the accidental ingestion of broken seeds of nux vomica usually in villages. It mimics tetanus, but the onset in this case is sudden and in between spasms the muscles are completely relaxed. A history of intake of the above is usually present. Chemical analysis reveals the poison.

d) Hypocalcemia & Hypomagnesemia

These may present with seizures, tremors and laryngospasm. Hypocalcemia may present as neonatal tetany but generalised rigidity and trismus are absent. Blood levels of calcium & magnesium clinch the diagnosis

e) Neonatal hypoglycemic convulsions

Here the patient presents with symptoms of irritability of the C.N.S., manifested by jitterness, coarse tremors, twitchings and convulsions. The neonates may also present with refusal of feeds, apathy, limpness and coma. Blood glucose estimation will be diagnostic. Also, there will be a prompt disappearance of symptoms on administering intravenous glucose solutions.

f) Phenothiazine & metoclopramide toxicity

These may manifest as pseudotetanus producing dystonic reaction and features of extrapyramidal rigidity manifested by spasm of the muscles of the back and neck, trismus and dysphagia. The rapid tonic siezures of tetanus are not found in individuals suffering from such a toxicity. A careful history of drug intake and metabolic studies of blood and urine are diagnostic.

g) In Intracranial haemorrhage and Kernicterus trismus is absent. The patient is jaundiced in kernicterus. An altered sensorium is present in these conditions (in tetanus the patient is alert). C.S.F. findings and serum bilirubin levels are diagnostic.

Organism and Pathogenesis

The Clostridium tetani is a 2-5 micron long and 0.3 to 0.8 micron wide, anaerobic, gram positive, motile, spore bearing bacillus. Spores are usually at the terminal end of the bacillus which impart a drumstick appearence to the organism.

The organism releases two types of exotoxins (1) Tetanospasmin and (2) Tetanolysin. However it is mainly the former that produces the neurotoxic effects.

Tetanospasmin is a selective neurotoxin which is a water soluble, easily diffusable protein, having a molecular weight of nearly 67000. Tetanospasmin acts on the motor end plates of skeletal muscles, spinal cord, brain and sympathetic nervous system (Kerr 1968).

Pathways of tetanus toxin to C.N.S.

There is a neural transport of the tetanus toxin into the Central Nervous System (C.N.S.), (Marie and Morax, Fedinec, Kryzhanovsky). The toxin spreads by the neural pathway with a definite rate depending on the quantity in the muscles, the particular features of the neural pathway and the muscle activity.

The neural pathway of the spread of toxin to the C.N.S. has the following links: Neural motor endings in muscles - Muscle nerve - Anterior roots- Anterior horns of the grey matter of spinal cord or motor-nuclei in the brain stem (Kryzhanovsky).

The toxin enters the C.N.S. by two pathways -

1) Regional neural pathway
2) General neural pathway

The clinical features of the disease greatly depend on the pathway which has been involved in the toxin

transport to C.N.S. If the toxin enters by the regional neural pathway there arises a local and ascendens tetanus in animals and partial tetanus in humans. Such a condition may arise if the toxin spread is blocked by antitoxins.

The general neural pathway represents the sum of regional neural pathways from all the muscles. When the toxin enters the blood, it enters all the muscles and then through the general neural pathway enters the C.N.S. In such a condition the toxin first enters the motor nuclei and travels through the shortest neural pathways to the muscles of head and face, imparting the typical features i.e. trismus and risus sardonicus. The toxin enters the C.N.S. by longer neural pathways to produce opisthotonos and generalised rigidity. This is known as tetanus descendens (Kryzhanovsky, 1966). However more important than this descendant phenomenon is the sequence of involvement of motor nuclei into intoxication in relation to the length of their neural pathway (Kryzhanovsky).

Toxin binding by brain tissue

The physico-chemical receptor of tetanus toxin in brain substance is represented by gangliosides for-

ming a complex with the cerebrosides (Heyningen, 1959), aided by the sialic acid in gangliosides (Mellanby et al, 1967). The toxin possesses three functional groups (Bondartchuk N.G. et al, 1973). (1) Antigenic - ensures binding of toxin with antitoxin. (2) Neurotropic-ensures binding with brain receptors or gangliotropic. (3) Toxophoric - ensures its pathogenic effects.

Binding of toxins by neuronal membranes

Synaptosomes have the greatest affinity for toxin binding. This is probably due to the reason that the membrane of synaptosomes contain gangliosides.Toxin neutralized by antitoxin is also bound by synaptosomes.

Effect of tetanus toxin on the Presynaptic Apparatus

Tetanus toxin acts on the presynaptic apparatus of central synapses in the spinal cord (Curtis et al,1968) and on the neuromuscular junction (Kryzhanovsky). This causes the disturbance of transmitter release, at the neuromuscular junction and central synapses, both for the neuromuscular excitatory transmitter (acetylcholine) and the central inhibitory transmitters - glycin and G.A.B.A.

Tetanus toxin has a universal effect on the presynaptic apparatus of various synapses and doesnot depend on the nature of synapse. In tetanus intoxication the affe-

cted neural tissues show a disturbance of transport of A.T.P.'ase. Under such a situation, the toxophoric group of toxin is activated, which might then split off and penetrate the neuronal membrane (Kryzhanovsky).

Functional effects of tetanus toxin on synaptic apparatus

A disturbance of the transmitter release by the presynaptic apparatus causes a block of synaptic transmission in tetanus intoxication.

The characteristic effect of tetanus toxin on C.N.S. during the course of its action, is the disturbance of the functioning of inhibitory synapses and the resulting block of various forms of postsynaptic and presynaptic inhibition (Kryzhanovsky). This causes a disturbance of segmental as well as of some forms of descendant inhibition in the spinal cord.

Pathogenesis of muscle rigidity and generalised convulsions

Muscle rigidity and generalised convulsions are produced by the basic mechanism of disturbance of inhibitory processes.

Muscle rigidity

This occurs due to the disturbance of inhibitory processes in the efferent output system of the spinal cord (i.e. in the motoneurons and the associated interneurons).

This results in an increased efferent output, enhanced polysynaptic reflexes and the periphery receives a strengthened and nearly permanent flow of efferent impulses. This results in a growing muscular tension, contraction and hypertonicity. This is attributed to the hyperactivity of the alpha motoneurons (Kryzhanovsky). Recently gamma system has been implicated in the pathogenesis of tetanic muscle contractions (Takeno et al, 1973).

Convulsions

The disturbance of the inhibitory mechanisms in the spinal interneurons causes convulsions (Kryzhanovsky).

Groups of spinal interneurons with disturbed inhibitory processes following the action of toxin become generators of "Universal dispatch station" (pathologically potentiated excitation), following triggering stimuli (afferent flow from tetanus limb). This spreads over the whole C.N.S. to produce generalised convulsions (Kryzhanovsky).

Functional changes in the Vegetative (Autonomic Nervous System)

A state of sympathetic hyperactivity due to the affection of sympathetic nervous system by the tetanus toxin occurs (Kerr et al, 1972). This results in tachy-

cardia, changes in arterial pressure, increased basal metabolism, intense perspiration, hyperthermia etc. However it is thought that an imbalance in the autonomic nervous system rather than hyperactivity of the sympathetic system is responsible for this (Kryzhanovsky). In neonates Sympathetic overactivity has been not described (Wesley A.G. et al).

Changes in the endocrine system

Tetanus intoxication effects the hypothalamo-hypophyseal system. In tetanus there occurs a water and electrolyte imbalance (Nikhailov, 1968). Catecholamine levels in hypothalamus are increased. There is a peculiar lack of glucocorticoids and noradrenaline in the tissues (Zorkin et al 1972).

Important visceral changes:

Pulmonary complications

Pulmonary complications in tetanus are one of the most common causes of death. Special investigations carried out by Kryzhanovsky et al, show that ultrastructural and microcirculatory changes in lungs are serious concomitants of tetanus intoxication. These lead to extensive pulmonary congestions (erroneously considered sometimes as pneumonia). Pulmonary complications also result from coagulation changes in pulmonary vessels, trophic disturbances in pulmonary

tissue and fall of pulmonary resistance.

Myocardial changes

A complex myocardial change takes place in tetanus. This consists of protein and vacule dystrophy, inhibition of the activity of oxidative restorative ferments (in particular of succinyl dehydrogenase), distubbance of microcirculation, intravascular thrombosis, perivascular haemorrhage and disturbance of lymphocirculation (Kryzhanovsky et al.). Under experimental conditions tetanolysin is found to produce changes in heart activity. However the immediate effect of the toxin on the myocardium remains open.

Mode of infection in tetanus

Tetanus occurs due to inoculation of the wound by tetanus spores which are present in the soil, dust etc. Soil enriched with manure, used in agricultural fields contain animal faeces and form a rich source of Clostridia. Certain accessory factors include trauma, haemorrhage, necrosis, chemical damage to tissues and infection by other microbes. These help in the germination of spores by producing anaerobic conditions in the defenceless tissues which might also be necrotic.

Improperly sterilized surgical instruments or dressings may harbour tetanus bacilli as well as the

contaminated dust of operation theatres. Catgut (infected) has been indicated as a source of post operative tetanus (Savolainen, 1950). Tetanus may also follow burns, ear infections, dental infections, abortion and pregnancy. Neonatal tetanus usually follows umbilical sepsis caused by improper handling of the cord, with unsterile techniques during labour. Spores may survive in the body for months to years and may result in the disease after some minor trauma which alters the local condition (Tullock, 1919).

Clinical forms of tetanus

Tetanus may be of three clinical types.

1) Localised tetanus

This results from the localised involvement of a group of muscles of a limb resulting in pain and spasm of muscles in proximity to the site of injury. Localised tetanus may convert into generalised tetanus.

2) Generalised tetanus

This results due to the generalised tonic rigidity and reflex convulsions. Trismus is the first indication of tonic rigidity and usually the first symptom. Spasm of the massetters leads to lock jaw, that of the facial muscles causes risus sardonicus. Tonic contraction of the abdominal and spinal muscles causes opisthotonos. Generalised convulsions appear as the severity increases.

3) Cephalic tetanus

This usually follows injuries of the head or face, especially around the orbits, though it can occur in cases with injuries to other parts and also without any apparent wound. Mortality is low and it carries a good prognosis (owing to its localised nature), Vakil et al. Cephalic tetanus usually remains confined to the head or neck though at times it may involve the entire body.

Prevention of tetanus

Tetanus is a preventable disease. It has in fact been suggested by some authors that it can be virtually eliminated by universal immunisation. This unfortunately is lacking in our country in the real sense. Consequently there is a high incidence of tetanus in India and particularly in Uttar Pradesh and the adjoining areas of Madhya Pradesh.

Two forms of immunization are available against tetanus.

1. Active immunization 2. Passive immunization.

1. Active immunization

This results in a much longer period of immunity as compared to passive immunization. But on the other hand active immunity takes a longer time to

develop. Immunity is conferred late to the patient, unfortunately lacking when the patient needs it most, whereas passive immunity provides immediate protective antibodies against tetanus, to the patient.

Two vaccines are available for active immunization (1) Plain tetanus toxoid

(2) Adsorbed vaccine

Though plain tetanus toxoid is a quite effective vaccine, the incorporation of an immunoglogical adjuvant in the vaccine such as aluminium hydroxide confers a number of advantages on this adsorbed vaccine -

(i) The immunity develops more quickly after using adsorbed toxoid. Immunity develops within 4 to 5 weeks of administration of adsorbed vaccine (Smith J.W.G.), while the plain variety may take a longer time.

(ii) The immunity stimulated by the adsorbed toxoid reaches a higher level and is longer lasting than the plain toxoid.

(iii) When administered concurrently with passive immunization, the adsorbed toxoid is more reliable. With plain toxoid, the injected antitoxin may interfere with the development of active

immunity, but interference with aluminium hydroxide adsorbed toxoid is minimal (Smith J.W.G.).

Plain tetanus toxoid consequently finds little place nowadays in tetanus prophylaxis as the adsorbed vaccine stimulates a quicker, higher and more durable immunity than plain toxoid.

Reactions to Tetanus Toxoid

These may be generalised or localised but are relatively uncommon. Local reactions were found to have a higher incidence in women as compared to men (White).

Generalised reactions may manifest as fever malaise etc. but are uncommon. Reactions resembling anaphylaxis or serum sickness are very rare.

Local reactions to tetanus toxoid are not serious and usually consist of local pain and tenderness accompanied with an area or visible erythema and swelling between 2 and 5 cms in diameter usually. Sometimes such reactions may become more marked with tenderness or swelling of the whole of the upper arm (where it is usually injected). However these reactions usually subside within 2-3 days.

Immunization schedule against tetanus

This process should be started right from the stage of pregnancy when the fetus and motor are

both provided with immunity by vaccination of the mother. Transplacental passage of maternal antitoxin prevents tetanus neonatorum. The active immunity produced in the mother prevents post partum/ abortal tetanus. The accepted protective level of antitoxin titre is 0.01 I.U. of tetanus antitoxin per millilitre of cord blood (Maclennan et al).

In pregnancy, the recent schedule for immunization is the administration of two doses of adsorbed tetanus toxoid, the first at 7 months of pregnancy and the second at 8 months.

In the newborn child the first dose of vaccine in the form of D.P.T. (triple vaccine) should be administered within 2 to 3 months of birth. It should be followed by two more doses at 4 to 6 weeks interval. A 4th dose should be given after one year of third dose. A booster is required at intervals of 10 years. School going children should be immunized with 3 doses of tetanus and diptheria toxoid starting from the age of 5 years, if already immunized earlier during infancy (even earlier if unimmunized before). The second dose should be given at 4-6 weeks after the first dose and the third dose 6 months to 1 year after the second dose. A booster is required every

6 to 10 years (Smith et al). In adults also a similar regime is followed starting at any age, as required.

A newer type of vaccine containing 3 times more potency (17.5 Lf as compared to normal 5 Lf by the ordinary toxoid) has been found to be very effective by only a single dose of toxoid. It takes 12 months for appropriate protective response to develop (Bfeman et al 1981).

Recently Talwar (1985) has developed a double acting vaccine against pregnancy and tetanus. Such a vaccine produces antibodies acting against Human chorionic gonadotropic hormone and also against tetanus toxin.

Passive Immunization

This is available in two forms

1) The equine antitoxin (A.T.S.) antitetanus serum.
2) Human antitetanus immunoglobulin.

This type of immunization confers immediate protection against tetanus and is particularly useful in tetanus prone situation, especially after exposure. The human form (T.I.G.) is devoid of any reaction or complications whereas the equine form (A.T.S.), dose produce at times severe sensitivity reactions and anaphylaxis. It is therefore administered after

appropriate sensitivity tests. Unfortunately the protection provided by passive vaccination is very short lasting.

Human anti tetanus immunoglobulin (T.I.G.) is administered in a dose of 250 I.U. i.m.deep. It ensures serum antibody levels of 0.01 unit/ml in all patients for 28 days or more. This may be combined with adsorbed tetanus toxoid (in a dose of 10 Lf) for active-passive immunization.

A.T.S. (antitetanus serum) is administered in doses of 1500 I.U. to 6000 I.U. i.m.after sensitivity tests.

Management of tetanus cases

Investigations

A differential count examination of W.B.C. reveals granulocytosis in one-third of the patients.
Microscopic examination of pus or necrotic material may reveal bacilli (tetanus) with spores in 30% of cases.
Culture methods are more reliable.
Sometimes raised levels of Serum Aldolase and Serum Creatinine phosphokinase are found. These may be diagnostic (Mullan et al 1964).
An electrocardiographic record usually shows sinus tachycardia.

Therapy

The treatment policy in tetanus is as follows-

I. (a) Neutralisation of unfixed toxins-tetanus antitoxin (T.I.G./A.T.S.).

(b) Elimination of the toxin source-local measures.

(c) Control of convulsions and muscle rigidity.

(d) Maintenance of adequate airway and ventilation.

(e) Symptomatic treatment and nursing care.

(f) Treatment of complications.

II. Prevention of recurrence.

III. Prophylaxis.

Neutralisation of the toxin

Antitetanus serum (A.T.S.)

Over the years tetanus antitoxin in the form of equine antitetanic serum (A.T.S.) has been used by various routes for the treatment of tetanus. Sherrington (1917) demonstrated the efficacy of intrathecal A.T.S. in monkeys. Ildirim(1974) & Sanders et al (1977) noted the efficacy of intrathecal A.T.S. along with parentral steroids in humans. However some have doubted its usefulness. Negquaye et al found that A.T.S. failed to improve survival in neonates despite its intrathecal use.

Bryant and Fairman (1940) were of the opinion that A.T.S. has a controversial role in tetanus therapy

besides producing allergic reactions. Damage to the C.N.S. by the preservatives used in it have discouraged its use. Pratt even suggested that intrathecal administration of A.T.S. should be stopped.

It has been suggested that antitetanus serum (A.T.S.) does not neutralize tetanus toxin already fixed in the C.N.S. and does little to ameliorate symptoms already present.

Human Antitetanus immunoglobulin

This sepcific antitetanus hyperimmune globulin (human) is obtained by fractionation of Hepatitis-B surface, antigen and AIDS antibody negative plasma, of human donors hyperimmunized with tetanus toxoid. This immunoglobulin is further purified by affinity chromatography, column chromatography and gel filteration techniques. Optimal purity of above 99% can be obtained. This is tested by immunoelectrophoresis.

Presentation

Anti tetanus human immunoglobulin (T.I.G.) is available in two strengths (1) Ampoules containing T.I.G.in a liquid form of 250 I.U. strength (2) Vials containing 500 I.U. of T.I.G. in a freeze dried powder form, along with diluent.

Advantages of Antitetanus human immunoglobulin

1) There is no risk of sensitization to heterologous protein - since T.I.G. is of human origin it is virtually free from the risk of inducing hypersensitivity reactions, unlike A.T.S.which is of equine origin,containing heterologous protein and hence having greater risk of hypersensitivity reaction.
2) Antibody levels of the homologous (Human) T.I.G. persist considerably longer than the heterologous (equine) A.T.S. The half life of T.I.G. is 20 to 40 days, while it is only 7 to 14 days in case of A.T.S. Hence T.I.G. protects longer.
3) Antitetanus human immunoglobulin doesnot interfere with patients antibody production.
4) It does notrequire sensitivity tests.
5) T.I.G. is devoid of any preservative and lypphilised.

It can be thus used intrathecally..

For therapeutic purposes 3000 I.U. to 6000 I.U. of T.I.G. have been recommended (Behrman et al, 1983) deep intramuscularly. For more rapid action part of this can be given intrathecally. In children some authors have recommended a dose of 4 units/kg body weight. However it is logical to administer at-least 250 I.U. regardless of age of the child, since theoretically the same amount of toxin will be produced in

in the child by the clostridia as in adults. Gupta et al (1980) recommended a dose of 250 I.U. intrathecally.

Varying results have been reported on the use of intrathecal T.I.G. Gupta P.S. et al (1980) found that intrathecal T.I.G. was useful in reducing mortality in patients with mild tetanus. He found that in patients who were given T.I.G. by i.m. route had a higher mortality. Chopra et al (1986) pointed the usefulness of intrathecal T.I.G. in high doses in more severe cases of tetanus.

Agnihotri et al (1984) also showed a reduction in mortality with intrathecal T.I.G. It also reduced hospital stay.

Contrary to the above Vakil et al (1977) found no difference in mortality in adult tetanus patients who received intrathecal T.I.G. Chugh et al (1985)also found no beneficial response of intrathecal T.I.G. in neonatal tetanus. McCraken (1971) pointed that there was no significant difference in mortality by intramuscular T.I.G. over intramuscular A.T.S.

It has been postulated that the initial spasms are due to the tetanus toxins circulating free

in the C.S.F. not yet fixed to anterior horn cells. Thus free toxin is available for neutralisation by intrathecal tetanus antitoxin which circumvents the blood brain barrier. But probably after 48 hours when the toxin is presumed to be fixed to the nervous tissue, intrathecal antitoxin is not of much value (Sanders et al).

Other uses of T.I.G.

- It is useful in all tetanus prone wounds as in crush injuries, compound fractures and accidental cases particularly if there is no clear evidence of prior immunization.
- In pre-operative preperations especially in emergency surgery.
- In uncovered cases of M.T.P. and septic abortions.
- In previously unimmunized mothers, when given during the antepartum period prior to delivery it provides dual protection to the mother and fetus. T.I.G. being 75 type crosses the placental barrier, giving protection to the fetus besides the mother.

Elimination of the toxin source - local measures

This is a very important step in the management of tetanus. It has been suggested by some authors that if wound toilet is properly performed within 6

hours of injury it will destroy the spores. But wound toilet alone if performed after 6 hours fails to prevent tetanus. However, meticulous toileting is still essential to prevent further absorption of toxins. Proper wound debridement should be carried out as soon as possible. Grossly contaminated wounds need to be cleaned with hydrogen peroxide solution. Use of local antibiotics may also be effective. In case of suppuration all pus should be drained out and wound cleaned.

In neonates the umbilical cord should be handled with all aseptic and antiseptic precautions. The cord should be cleaned with spirit and 1% gention violet paint should be applied. Ear infections need to be taken care of promptly. Any discharge should be cleaned with spirit swabs and ear kept dry. Handling with dirty hands or entry of water and the instillation of any household medicament in the ear needs to be stopped. Appropriate antibiotic and if necessary local ear drops should be used.

Chemotherapy

Antibiotics notably Pencillin are quite effective against Clostridium tetani and their use similarly has been thought to affect the outcome

favourably (Percy et al).The usefullness of penicillin has also been suggested by Bhat et al (1979) and Bhandari (1980).

In a patient sensitive to penicillin, Kanamycin in two divided doses of 10 mg/kg body weight may be used.

Metronidazole is effective against anaerobic bacteria. Some have pointed its usefullness in the disease.

Control of convulsions and muscle rigidity

The control of muscle spasms is one of the most important factors in the prognosis of patients with severe tetanus.

Many muscle relaxants have been advocated but some have their own demerits. To name a few,-Centrally acting muscle relaxants like methocarbamol, mephenesin, meprobromate etc.; Peripheral muscle relaxants like d-tubo-curarine, succinylcholine, Mytolon etc. Peripheral muscle relaxants are usually administered alongwith I.P.P.V.

Mephenesin is an effective muscle relaxant when given intravenously. Its drawback is that it causes hypotension and sometimes haemoglobinuria (Parks).

Meprobromate has been described as one of the most effective drugs in relieving muscle spasticity (Nyguist et al). It has a prolonged action. However it has the disadvantage of causing thrombosis, hemolysis and possibly, glomerular damage on intravenous therapy.

Methocarbamol appears to possess the ideal pharmacological action to control the muscle spasm induced by tetanus toxin. It has a greater potency and acts for a longer duration (Crandall et al).

It has the added advantage of suppressing spasms without appreciable suppression of respiration. The dose is 2 to 20 gm per day by intravenous infusion or orally in divided doses.

Diazepam - In addition to being a hypnotic, diazepam is a potent muscle relaxant. It acts by depressing the ascending reticular activating system and intermuncial neurons. Diazepam was first used by Weinberg (1964). Hendrickse and Sherman found that diazepam was very effective in controlling convulsive spasms during the early phase of treatment. Kazim reported that intravenous diazepam relieved opisthotenos but the effect lasted slightly more than an hour. Benjamin and Baltimore recommended diazepam as an alternative to

phenoberbitel or phenothiazines. He found that parentral diazepam was very useful.

However a combination of muscle relaxants has been found to be more effective than massive dose of any single drug (Jolly et al, 1973). Diazepam was first used in combination with chlorpromazine by Hendrickse et al (1965).

Maintenance of airway and tracheostomy

Maintenance of a clean airway and adequate ventilation is of utmost importance in tetanus care. All secretions should be aspirated by suction. The mouth and nasal cavities should be kept as clean as possible. All froth should be cleaned. Children and neonates should be nursed with their head on one side to prevent aspiration of fluids into lungs. If necessary endotracheal intubation may be carried out. If it is not possible then tracheostomy should be performed. The indication for tracheostomy is either laryngospasm or copious secretions. Endotracheal suction can then be carried out. However care of tracheostomy is then required.

The need for tracheostomy should be recognised early and should rather be performed electively than as an emergency procedure. Shah et al (1984)

found a mortality of 19.26% with tracheostomy. However the drawback is that it needs meticulous post-tracheostomy care and trained nursing personnel for its management.

Oxygen inhalation should be given as and when necessary.

Total paralysis and ventilation

In severe tetanus complete muscular relaxation (paralysis with peripheral muscle relaxants eg. d-tubocurarine) combined with tracheostomy and intermittent positive pressure ventilation (I.P.P.V.) has been a landmark in tetanus therapy.

Lassen (1953); Smith et al (1956) and Hendrickse et al have reported favourably on the use of tracheostomy, total paralysis and I.P.P.V.

However only limited effectiveness has been claimed by Alhaudy et al, by this regime. Sinha and Athavale found this type of treatment unsuitable in India on account of its cumbersomeness, costs and the need of skilled medical and para-medical personnel.

General management and nursing care

The patients should be nursed in an isolated, quiet and calm environment to cut off all external stimuli. Adequate care of bowel, back and bladder is

required. Frequent turning in bed alongwith the application of powder and spirit to clean the back is necessary to prevent bedsores. The patient should be catheterized to avoid possible urinary retention and incontinence. Appropriate antibiotic coverage may be given and should be changed according to culture and sensitivity reports. Constipation should be taken care of with suppositories or low enemata as necessary.

Oral nutrition is maintained as far as possible However if dysphagia increases intravenous fluids are given and oral supplementation stopped till protective reflexes of swallowing and coughing are present. If necessary Ryles tube feeding may be supplemented.

As regards fluid requirements a minimum fluid intake of 130 ml/kg/day in children under 6 years and 80-130 ml/kg/day in older children has been recommended (Kerr J.H.). In adults the amount should be regulated in relation to urine output and fluid losses. This may vary from 1.5 to 4 litres per day as necessary under the circumstances.

Small daily fluid deficits may accumulate to produce subclinical dehydration (Kerr J.H. 1981). As such it may be produced by fluid losses in saliva and sweating. Hence it is important to maintain adequate hydration.

Other miscellaneous forms of therapy

Corticosteroids

Sanders et al have pointed the usefulness of steroids in tetanus therapy, in particular betamethasone.

The explanations given by them were that-

(1) Part of the action of betamethasone is antihistaminic. This results in reduction of pericellular oedema around motor nerves and ganglions.

(2) It is possible that betamethasone either reduces the amount of acetylcholine produced, or inhibits its action (Fal, W. et al (1963). Betamethasone may also support a failing suprarenal function (Sanders et al).

(3) Betamethasone may have an antitoxaemic action in tetanus.

Beta blockers

Sainani et al, found that the tetanus toxin has a beta stimulant effect on the frog's heart and this effect could be blocked by propranolol (beta-blocker). Kerr et al, observed that there was sympathetic overactivity in tetanus patients. This sympathetic overactivity manifested as disproportionate tachycardia, fluctuating high blood pressure and profuse sweating. Such patients having features of sympathetic overacti-

vity when treated with beta-adrenergic blocking drugs showed improvement (Kerr et al). Prys Roberts et al also observed beneficial effects of propranolol.

However the role of beta blockers is disputed and still under clinical trial. The literature now contains that remoting sympathetic stimuli to the heart may remove the ability to sustain adequate blood flow through the constricted peripheral vasculature (Edmonton R.S. et al).

Pyridoxine

Godet et al (1982), observed that pyridoxine hydrochloride in a dose of 100 mg per day by intramuscular route decreased tetanus mortality upto 15%.

Cholinesterase restoring therapy

Leonardi et al observed that the tetanus toxin had an anticholinesterase effect somewhat similar to organophosphorus agents and that antidotes to such agents, the oxime group of compounds could, by their cholinesterase restoring action, be of benefit in tetanus therapy. They used pralidoxime methanosulphonate 40 mg/kg/day together with vitamin B_{12} in a dose of 100 mg/kg/day for 10 days intramuscularly and found it to be of some benefit. But this still requires further trials.

Hyperbaric oxygenation

In a trial conducted by Pascale et al, it was observed that there was active regression of symptoms following hyperbaric oxygen therapy. The progression of the disease was arrested and reversed. However its use is limited, owing to its limited availability in hospitals. Furthermore, it requires more trials.

Prognostic factors

Age - Vaishnava et al found that the survival rate was influenced by the patients age. In children and adult patients he found that higher the age the worse was the prognosis. In neonates the lesser the age at the time of admission the worse is the prognosis (Phatak et al, Bhat et al).

Sex - Vaishnava et al, found no difference in the mortality in two sexes. Vakil et al (1974) also found a similar observation. However Modi (1965) found a higher mortality in males.

Incubation period - Mortality varies inversely with the incubation period. The longer the incubation period, the lesser is the mortality (Patel et al (1965), Vakil (1964).

Period of onset - Mortality increases with shorter period of onset (Patel et al (1959), Vaishnava et al (1966), Cole (1940).

Severity of convulsions - Mortality increases with increasing severity of convulsions (Bhandari et al (1980). Bhat et al (1979), Shrivastava et al, Shah et al).

Fever - Fever has been reported as a bad prognostic sign (Bhandari et al, Spaeth et al).

Complications and causes of death

Oversedation is one of the major complications of the treatment given (Sehgal et al).

Respiratory complications including aspiration pneumonia are very important and commonly encountered complications (Sehgal et al, Bhat et al, Athavale et al). Injection abscess may occur occasionally (Sehgal et al). Parotitis has also been reported by some workers (Athavale et al, Bhat et al). Other complications include hyperpyrexia, constipation, thrombophlebitis, electrolyte imbalance, bed sores, septicemia and retention of urine (Bhat et al).

Athavale et al have reported dehydration, acidosis, facial palsy and compression fracture of vertebrae as important complications.

Respiratory spasms with apnoeic spells are the commonest cause of death (Athavale et al, Bhat et al). Death may also occur due to hyperpyrexia, laryngeal spasms,

laryngeal or pulmonary oedema, electrolyte imbalance, hypoxia etc. However all of the above complications may contribute to death, although some of the complications may be reversed when diagnosed and treated early and the patient may be saved.

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MATERIAL & METHODS

MATERIAL AND METHODS

The present study includes tetanus cases admitted between January 1988 and December 1988, at M.L.B. Medical College Hospital, Jhansi (U.P.). 285 patients of tetanus of all age groups were admitted out of which 245 cases were studied and analysed (40 patients absconded or left against medical advice).

History

A detailed history of the patients, was taken with special reference to age, sex, address, religion, occupation, socio-economic status, customs and habits. The complaints were noted with special reference to the portal of entry of infection, duration of symptoms and their severity. The incubation period and period of onset could be thus calculated. Besides other complaints the presence or absence of the following symptoms was stressed upon. These included lock jaw/inability to suck (neonates) excessive crying (neonates), dysphagia, fever, posture (opisthotonous pleurothotonos, supine, flexed) and convulsions.

Any past history of infection or prophylactic immunization against tetanus, history of delivery,

burn, injury of operation was noted besides patients complaints.

In neonates, the place of delivery, the person who conducted the delivery (trained or untrained), instrument used for cutting the cord (sterile or unsterile) and any application over the cord was noted. Any history of antenatal immunization in the mother was noted.

Physical examination

This consisted of a general and local examination. The general examination included the general condition, consciousness, pulse, temperature, blood pressure, respiratory rate, hydration, the presence or absence of cyanosis, oedema, jaundice, lymphadenopathy constipation, retention of urine and any other systemic problem relating to respiratory, cardiovascular, abdominal, nervous or other sytems.

On local examination the following were noted-temperature, lock jaw, dysphagia, risus sardonicus, inability to suck, excessive crying, body and limb rigidity, posture, opisthotonus, pleurothotonous, neck rigidity and convulsions.

In neonates the following points were stressed upon-excessive cry, inability to suck, posture convulsions, rigidity, prematurity, umbilical sepsis, jaundice and kernicterus. The patients were divided in 3 groups according to age.

(1) Tetanus neonatorum

This included all neonates from birth to the age of 1 month.

(2) Childhood tetanus

This included all patients from infancy (above 1 month of age) to the age of 12 years in chilhood.

(3) Adult tetanus

All cases above the age of 12 years were put in this group.

Patients were also classified on the basis of the severity of disease based on Patel and Joag's (1959) criteria for the same.

Criteria (1) Presence of lock jaw/inability to suck.
" (2) Presence of spasms
" (3) Incubation period of 7 days or less
" (4) Period of onset - 48 hours or less.
" (5) Fever on admission i.e. axillary temperature of 99°F or Rectal temperature of 100°F on on admission or within 24 hours of admission.

The cases having one of the five criteria were termed as grade I, the cases having only two of the five criteria as grade II, cases having all of the five criteria as grade V and so on.

In some cases the incubation period could not be determined as no obvious cause was present. Patients with a prolonged history of ear discharge also presented the same problem. Incubation period could not be ascertained in such patients.

Therapy

The patients were admitted and nursed in the tetanus ward.

All the patients were put on the following regime -

(1) Local measures for elimination of toxin source.
(2) Administration of intrathecal anti-tetanus human immunoglobulin to neutralize unfixed toxins.
(3) Control of muscle spasms and convulsions.
(4) Maintenance of airway and ventilation.
(5) Symptomatic treatment and nursing care.
(6) Immunization (active).

Meticulous cleaning of wounds was done with antiseptic solutions. Wound debridement was done

where necessary. Hydrogen peroxide was used for grossly contaminated or necrotic wounds. Sepsis was taken care of and pus was let out by incision and drainage in case of suppuration. Ear infections were taken care of with proper cleansing, dry mopping and antibiotics. Dressings were changed as and when necessary. Oral hygiene was cared for. In neonates the umblical cord was cleaned with rectified spirit and 1% G.V. paint was applied. Antibiotics were also used locally as necessary in the form of ointments or powder.

Anticonvulsants and sedatives were used for the control of muscle spasms and convulsions. Diazepam was used for sedation, control of spasms and rigidity, in doses of 0.3mg to 1.0 mg per kg. of body weight in divided doses, according to the severity of rigidity and spasms. In adults 2 mg to 20 mg of the drug was given eight hourly or repeated even earlier at shorter intervals as required.

Where diazepam alone was not effective in controlling spasms promethazine was added in a dose of 50 - 250 mg/day as required alongwith other drugs.

Methocarbamol (Centrally acting muscle relaxant) was given alongwith diazepam in a dose of

100 - 200 mg/kg of body weight per day in divided doses.

Diazepam, phenargan and methocarbamol were used by the intravenous route, either by continuous infusion (slow) in intravenous drip solution, or intravenous as such if frequent doses were necessary. When the patients condition improved and if the patients could swallow, these drugs were given orally as tablets. The dose of sedatives and muscle relaxants was gradually tapered according to regression of rigidity, convulsions and other symptoms.

Adequate ventilation and patency of airway was taken care of, with frequent suction and cleaning of the oral and nasal passage. Intubation and tracheostomy were done when necessary. However tracheostomy did not prove to be of much benefit. I.P.P.V. was not used. Patients with dysphagia and frequent, repeated convulsions, were kept on intravenous fluids for maintenance and nutrition. Ryles tube feeding was started on regression of spasms. When lock jaw and dysphagia had decreased, to the extent that the patient had no requrgitation and chocking on swallowing and if he/she could open the mouth sufficiently, oral feeding was started.

Care of the back was done to prevent bed sores by frequent change of posture, cleaning with spirit and antiseptics and application of talcum powder (medicated). Bladder care was done. Retention of urine was avoided by early catheterization. Urine cultures and wound swab cultures were done and appropriate antibiotics instituted based on sensitivity tests. Bowels were taken care of by avoiding constipation. When necessary, glycerine suppositories, aperients & laxatives or enemata were used.

Initially all patients were administered crystalline penicillin in a dose of 50,000 to 1 lakh units per kg of body weight per day in 4 to 6 divided doses perentrally. Patients sensitive to penicillin were administered ampicillin, chloramphenicol or any other suitable drug.

In patients with super-added chest infection or gram negative sepsis gentamicin injection was given par-entrally in dose of 2 - 7.5 mg/kg of body weight in twice daily or thrice daily divided doses. Metronidazole (oral & i.v.) was used in some patients.

Therapy with intrathecal T.I.G.

All patients were given intrathecal human

antitetanus immunoglobulin (T.I.G.) in doses of 250 I.U. to 3500 I.U. Some patients were given T.I.G. intramuscularly as intrathecal administration failed in such patients. No other patient was given intramuscular T.I.G. Alongwith this the patient was given standard supportive therapy as already mentioned.

Owing to its expensiveness higher doses of T.I.G. could only be given to those patients who could afford it.

Procedure

Lumbar puncture was performed in the interspace between L_3 L_4 or L_2 L_3 vertebrae under all aseptic and antiseptic precautions and after mild sedation and relaxation of the patient with diazepam and methocarbamol. In case of the freeze dried powder, form of T.I.G. it was freshly prepared by the addition of diluent provided alongwith it. After introducing the lumbar puncture needle in the subarachnoid space 8 to 10 drops of cerebrospinal fluid was allowed to drain out slowly. T.I.G. was then slowly instilled intrathecally through the lumbar puncture needle.

Immunization

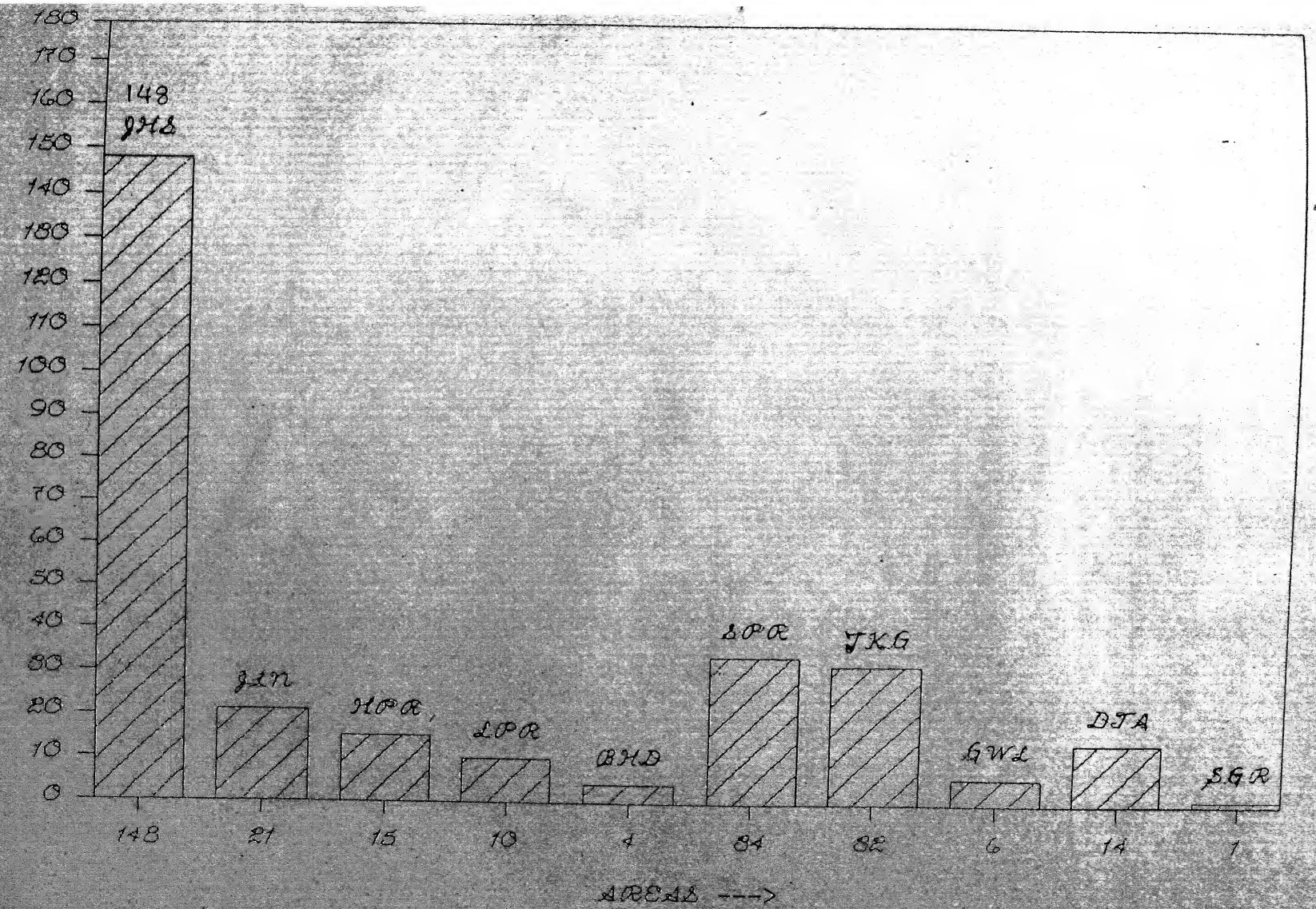
All patients were immunized with tetanus toxoid 0.5 ml. intramuscularly on admission. They were asked to report at 6 weeks and 6 months intervals for further two doses of immunization.

OBSERVATIONS

O B S E R V A T I O N S

The present study includes 245 cases of tetanus of all age groups admitted at M.L.B.Medical College, Hospital, Jhansi (U.P.) between January 1988 and December 1988 (alltogether 285 patients of tetanus were admitted out of which 40 patients left against medical advice).

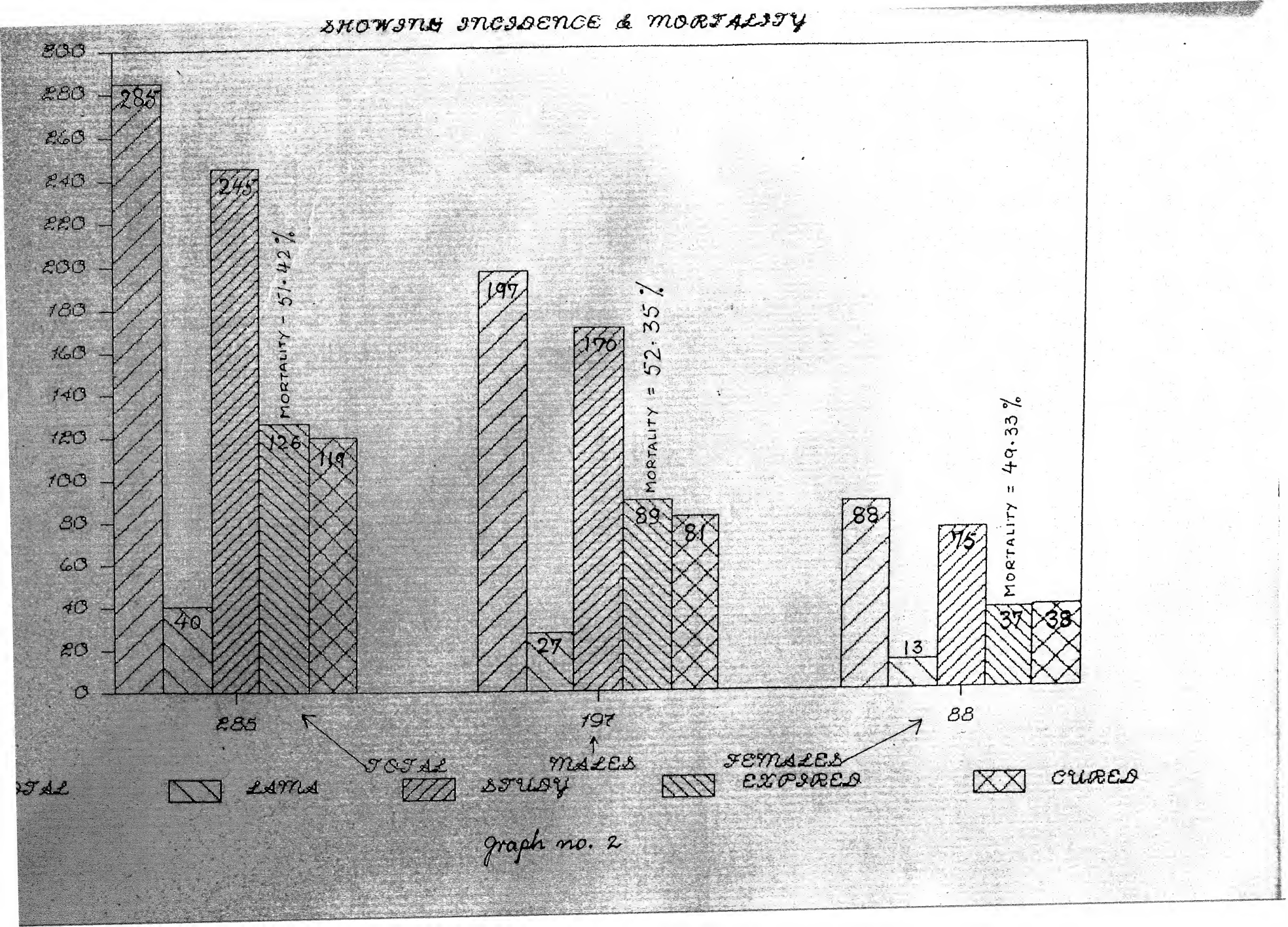
The following observations were made :


NUMBER OF PATIENTS
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
148
JHS
JLN
HPR
LPR
BHD
SPR
JKG
GWL
DTA
SGR
148
21
15
10
4
84
82
6
14
1
AREAS --->

Graph No. 1

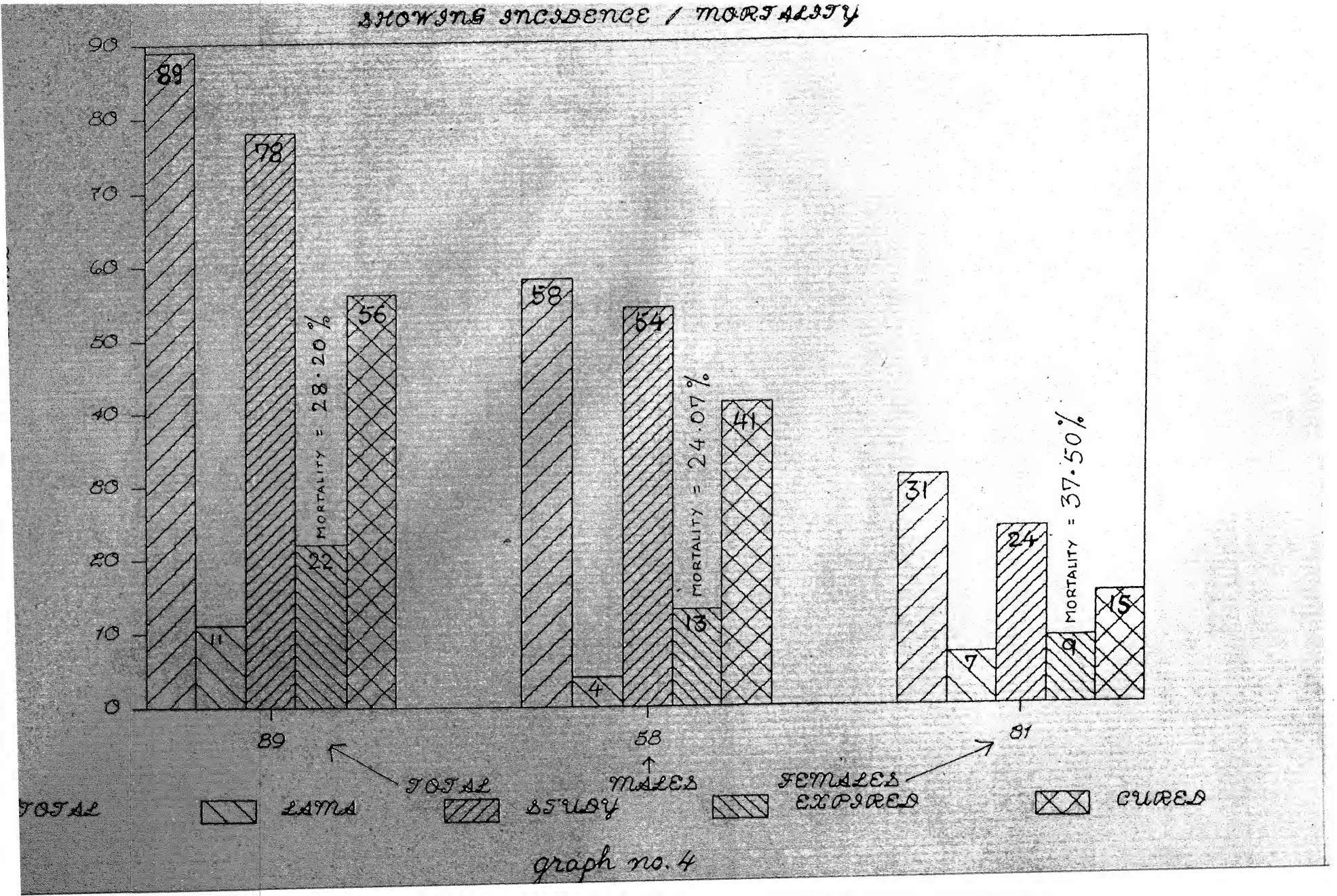
Graph No. 1 shows the area-wise incidence of tetanus in Bundelkhand region. It can be seen that the maximum number of cases were from Jhansi (U.P.)(148), followed by Shivpuri (M.P.) (34), Tikamgarh (M.P.) (32), Jalaun (U.P.) (21), Hamirpur (U.P.) (15), Datia (M.P.) (14), Lalitpur (U.P.) (10),Gwalior (M.P.) (6), Bhind (M.P.) (4) and Sagar (M.P.) (1) respectively.

SHOWING INCIDENCE & MORTALITY

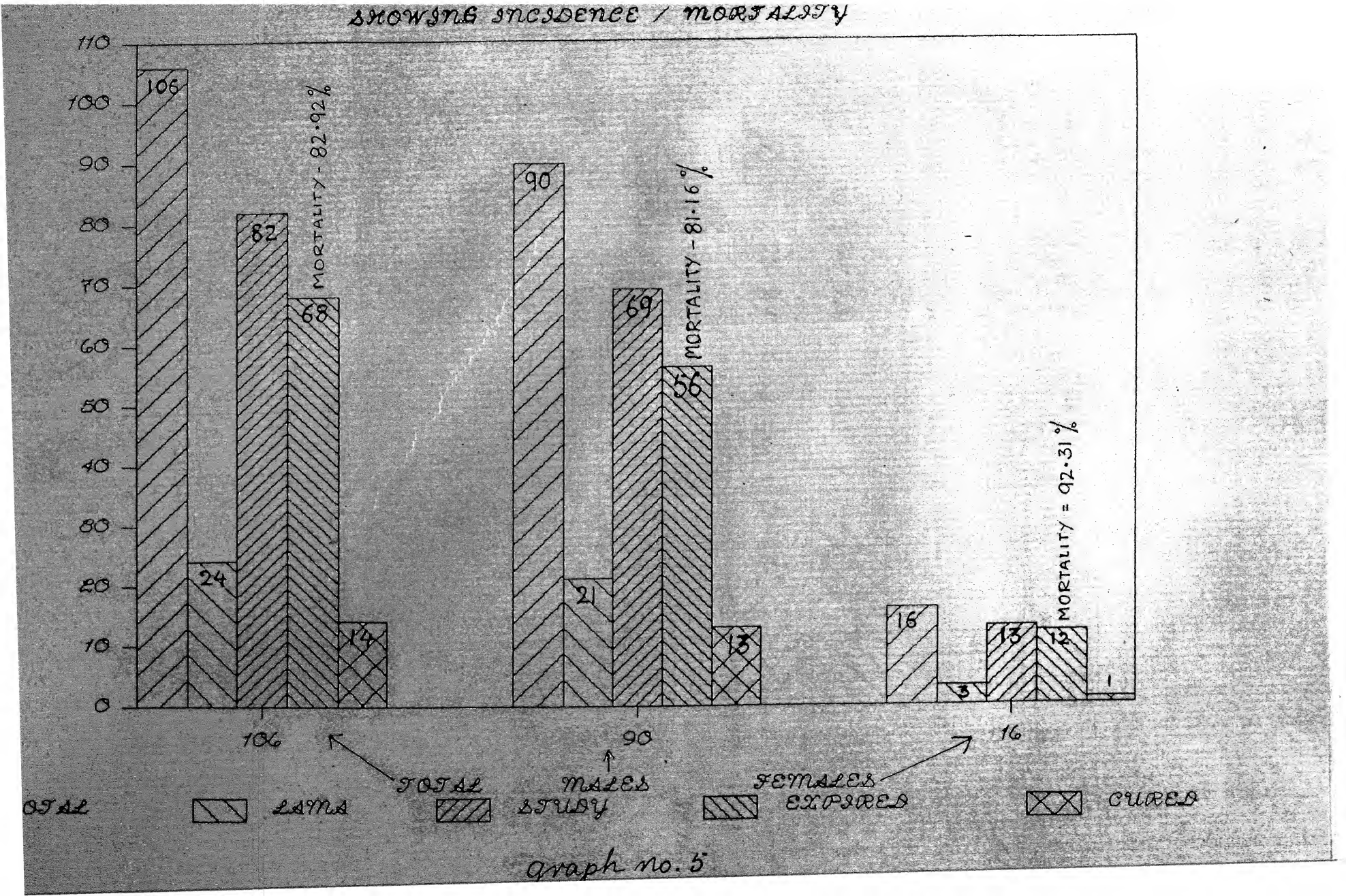


graph no. 2

NUMBER OF PATIENTS
TOTAL
PART
MORTALITY = 42·35 %
MORTALITY = 42·53 %
MORTALITY = 42·10 %
Graph No. 3


SHOWING INCIDENCE / MORTALITY
90
80
70
60
50
40
30
20
10
0
89
11
78
22
56
58
4
54
13
41
31
7
24
9
15
MORTALITY = 28.20 %
MORTALITY = 24.07 %
MORTALITY = 37.50 %
89
58
81
TOTAL
MALES
FEMALES
TOTAL
CAMA
STUDY
EXPIRED
CURED

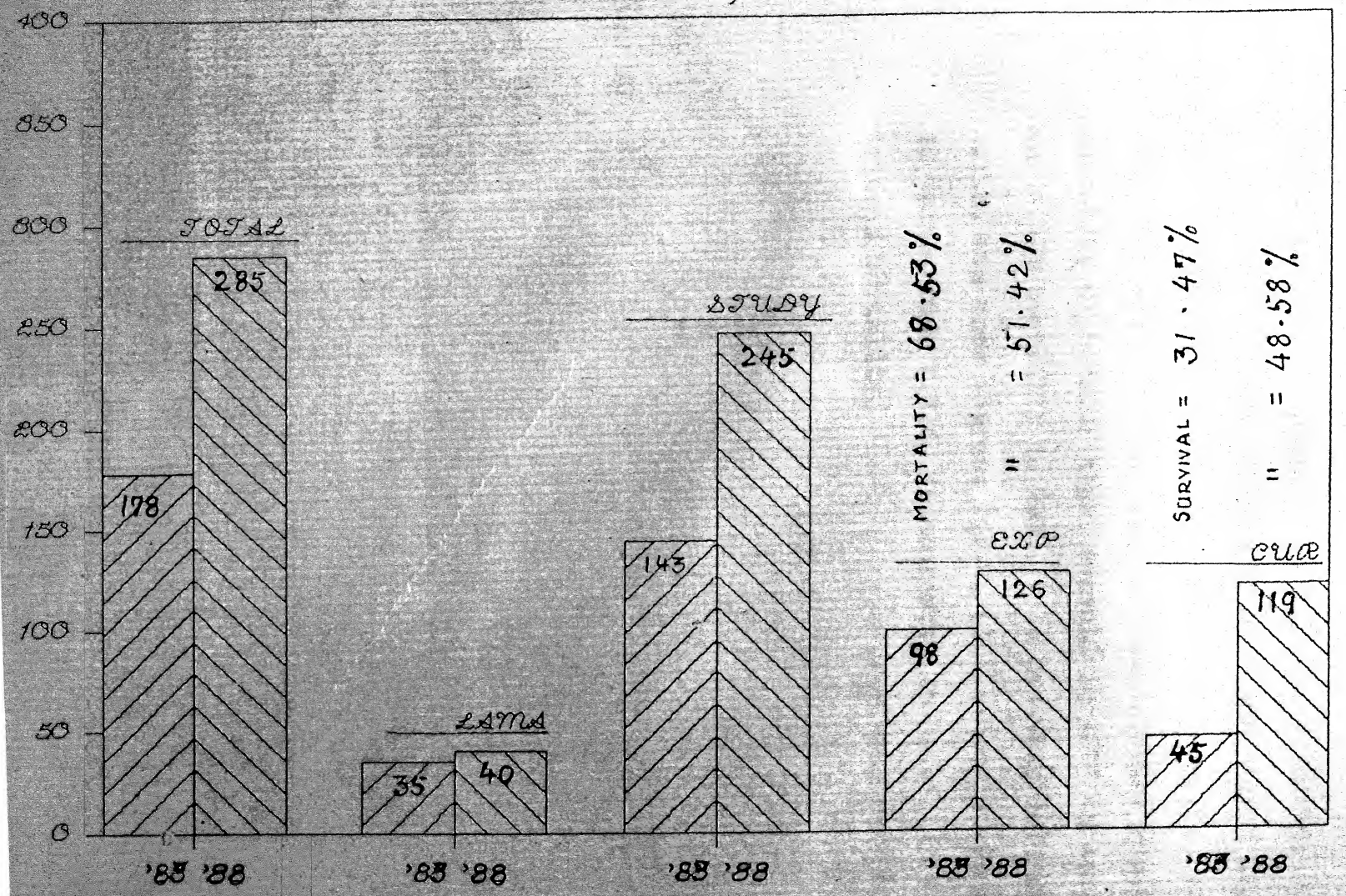
graph no. 4


SHOWING INCIDENCE / MORTALITY
110
100
90
80
70
60
50
40
30
20
10
0
106
24
82
68
14
90
21
69
56
13
16
3
13
12
1
MORTALITY - 82.92%
MORTALITY - 81.16%
MORTALITY = 92.31%
106
90
16
TOTAL
MALES
FEMALES
TOTAL
CASES
STUDY
EXPIRED
CURED

graph no. 5

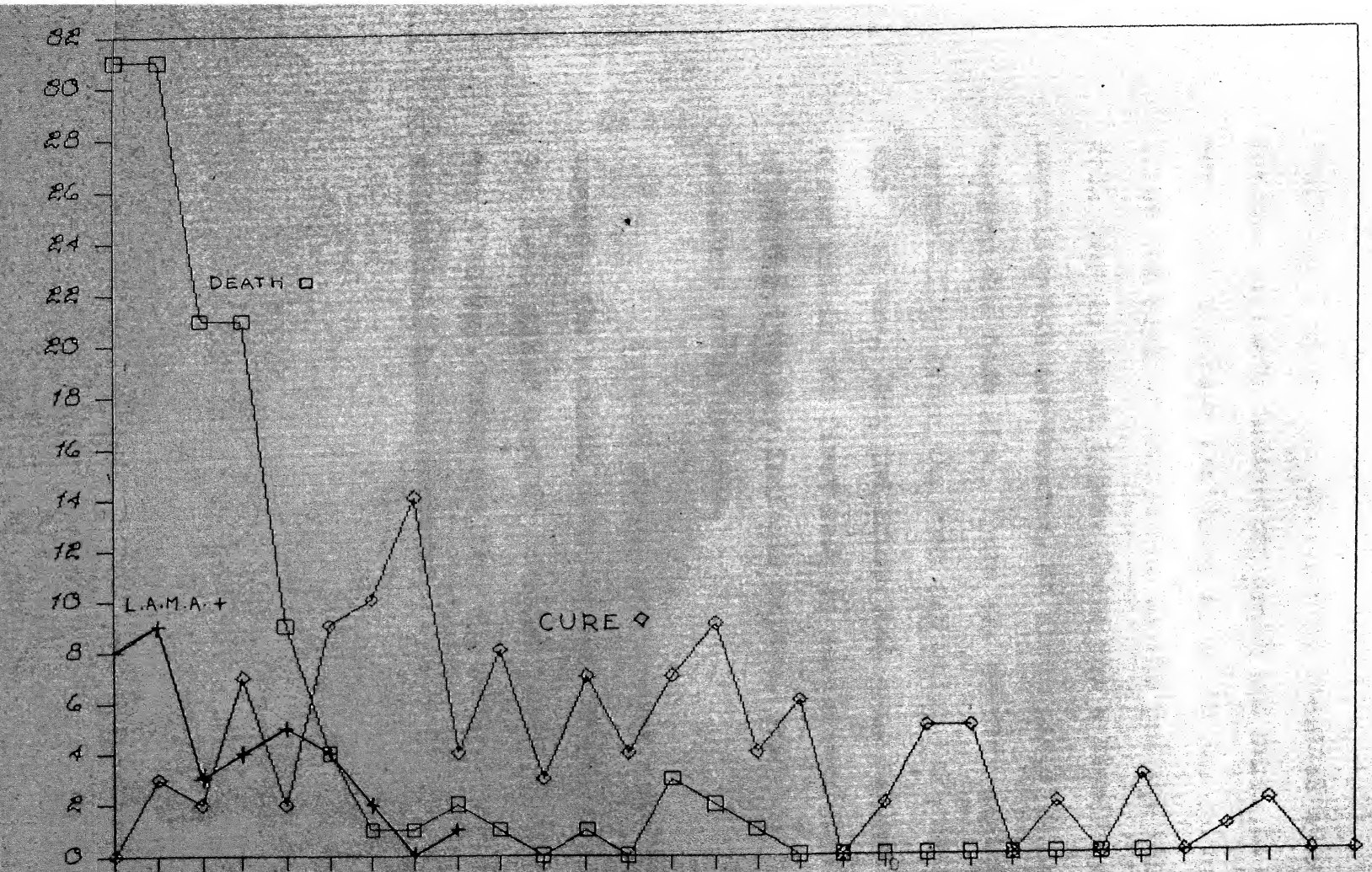
TETANUS INCIDENCE / MORTALITY

COMPARATIVE FIG. 1983/88



graph no. 6

Graph No. 6 shows comparative figures of incidence and mortality of the years 1983 and 1988. There was a higher incidence of tetanus in 1988 as compared to 1983 (285 and 178 cases respectively). There was 68.53% mortality of tetanus cases overall in 1983 as compared to 51.42% mortality in 1988. (In the year 1983 only A.T.S. was used whereas T.I.G. (intrathecal) was used in 1988). Thus T.I.G. is supe-rior to A.T.S. in reducing tetanus mortality.



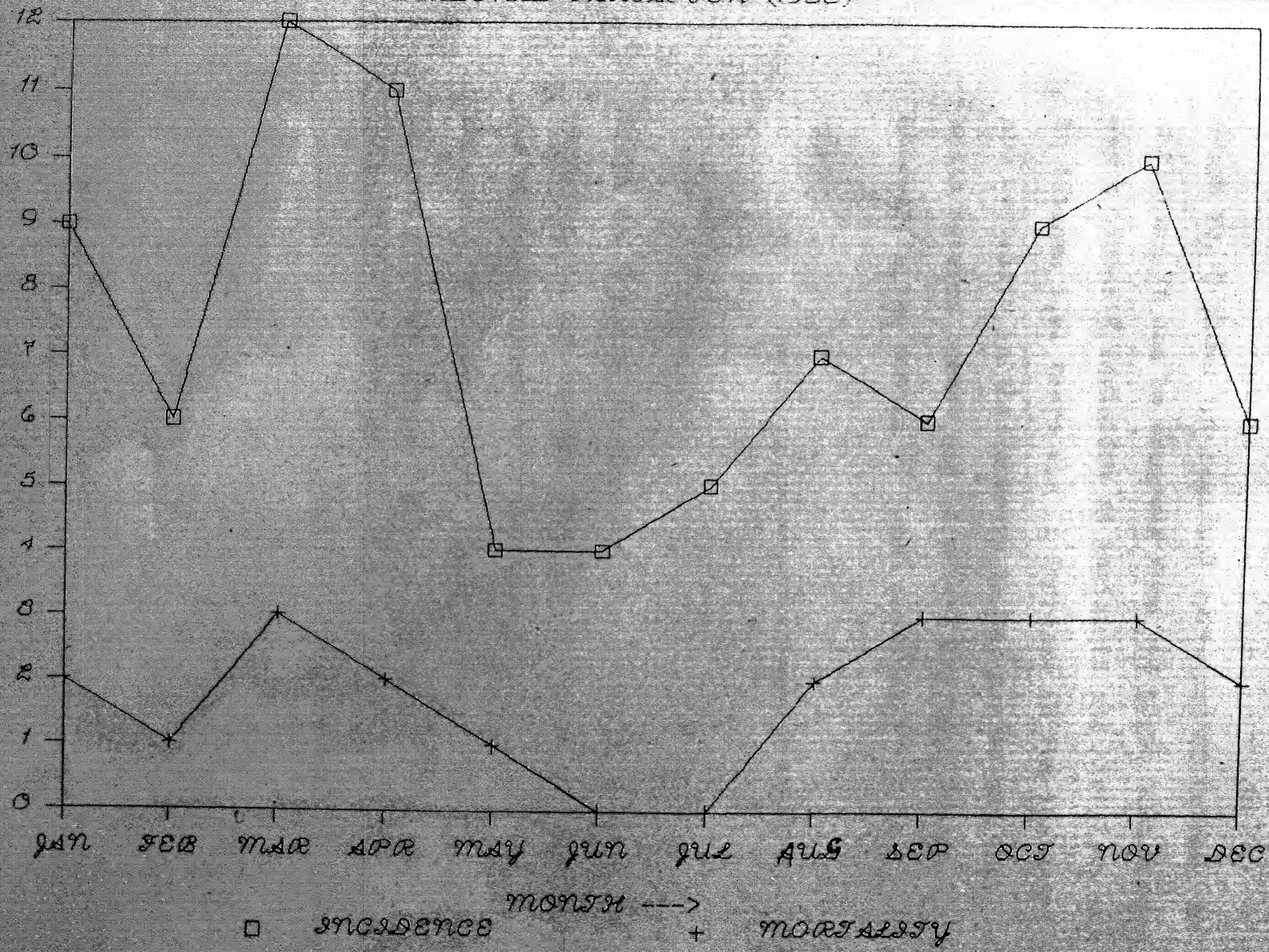
graph no. 7

Graph No. 7 shows the duration of hospital stay of tetanus patients indicating death and cure. It can be seen that the peak incidence of death was during the first two days of admission. On the 3rd and 4th day it fell down by about 1/3rd. There was a steady fall in mortality 4th day onwards. On about the 11th day it touched the base line. There was however a slight rise in mortality after the 13th day which fell down after the 17th day. This indicates that most tetanus deaths occur within the first week of admission. Deaths occuring after the 13th day indicate deaths, probably due to secondary complications.

Patients showed improvement, from 2nd day onwards, the maximum cure occuring between the 6th and 9th days. After that it remained nearly constant till the 17th day. After the 22nd day however there was a slight fall in the survival.

TETANUS IN CHILDREN

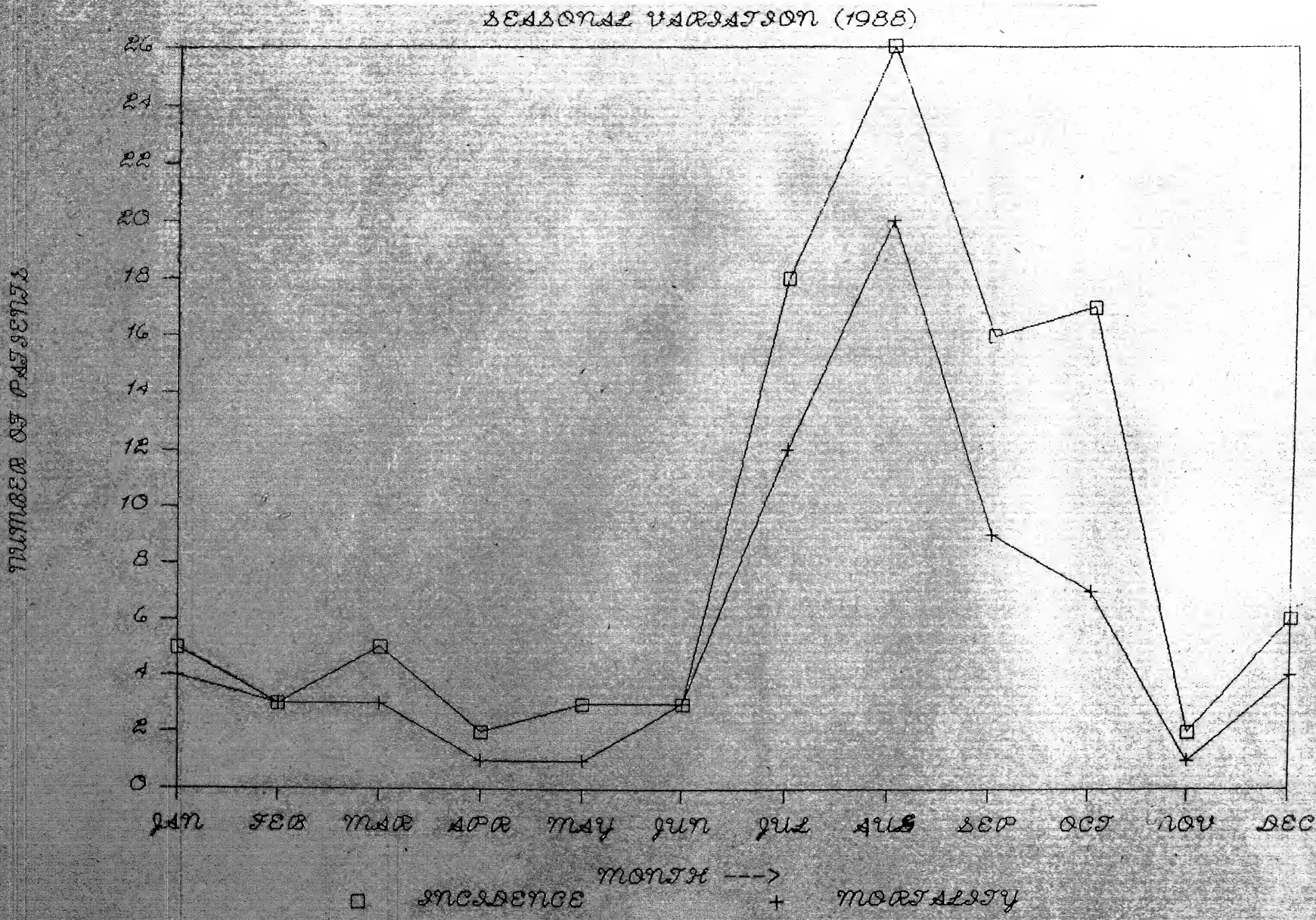
SEASONAL VARIATION (1988)



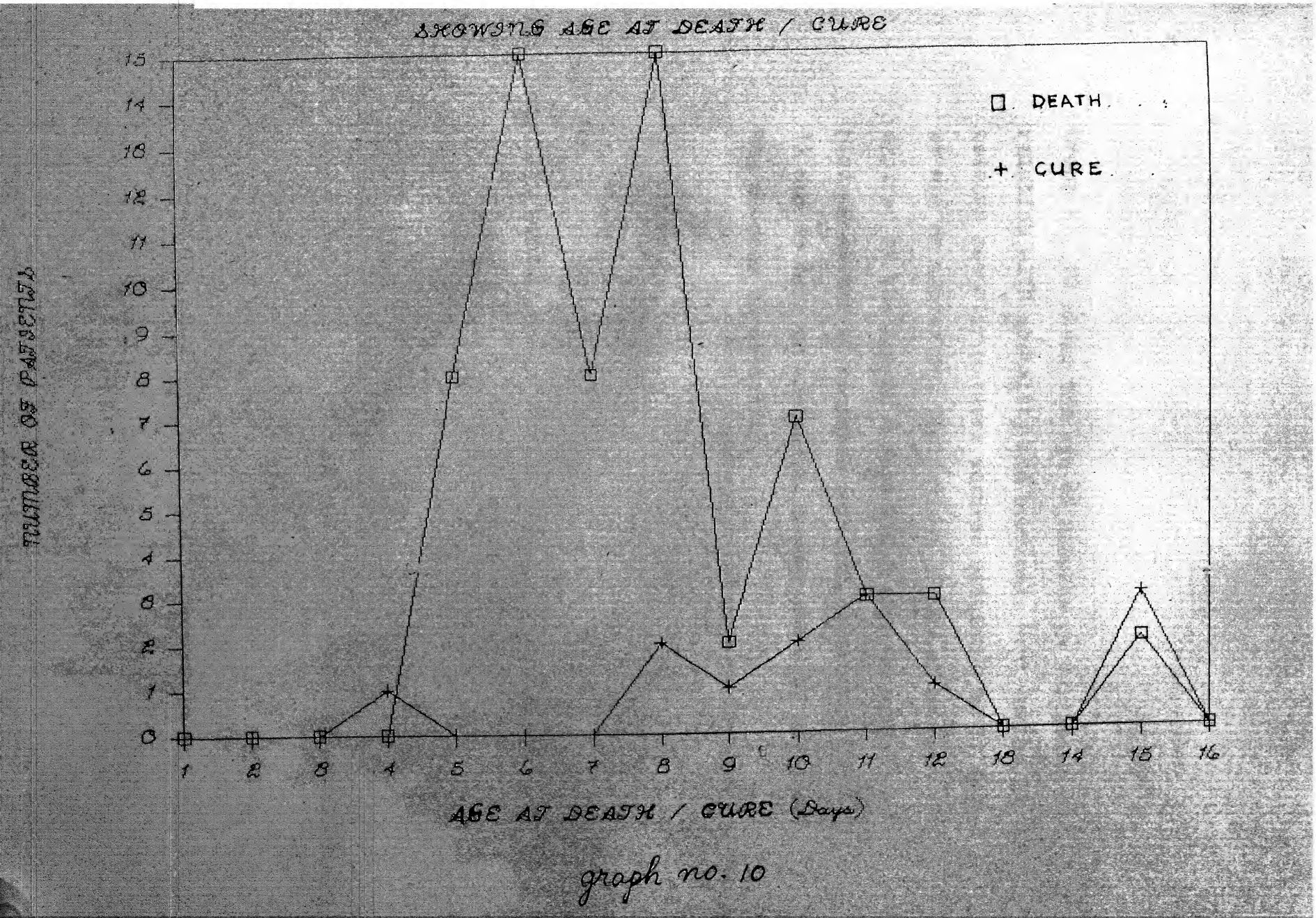
Graph No.8

Graph No. 8 shows the seasonal variation of tetanus in children. It can be observed from the graph that there was a biphasic variation of incidence and mortality due to tetanus i.e. there was an increase in the incidence and mortality in the February to May period and then again between August and December. The peak incidence was however in the months of March and April.

Graph No. 9 shows the seasonal variation of tetanus in neonates. It can be seen that the incidence and mortality was highest between June and November, the peak being in the month of August, which indicates that tetanus neonatorum is more prevalent during the rainy season.

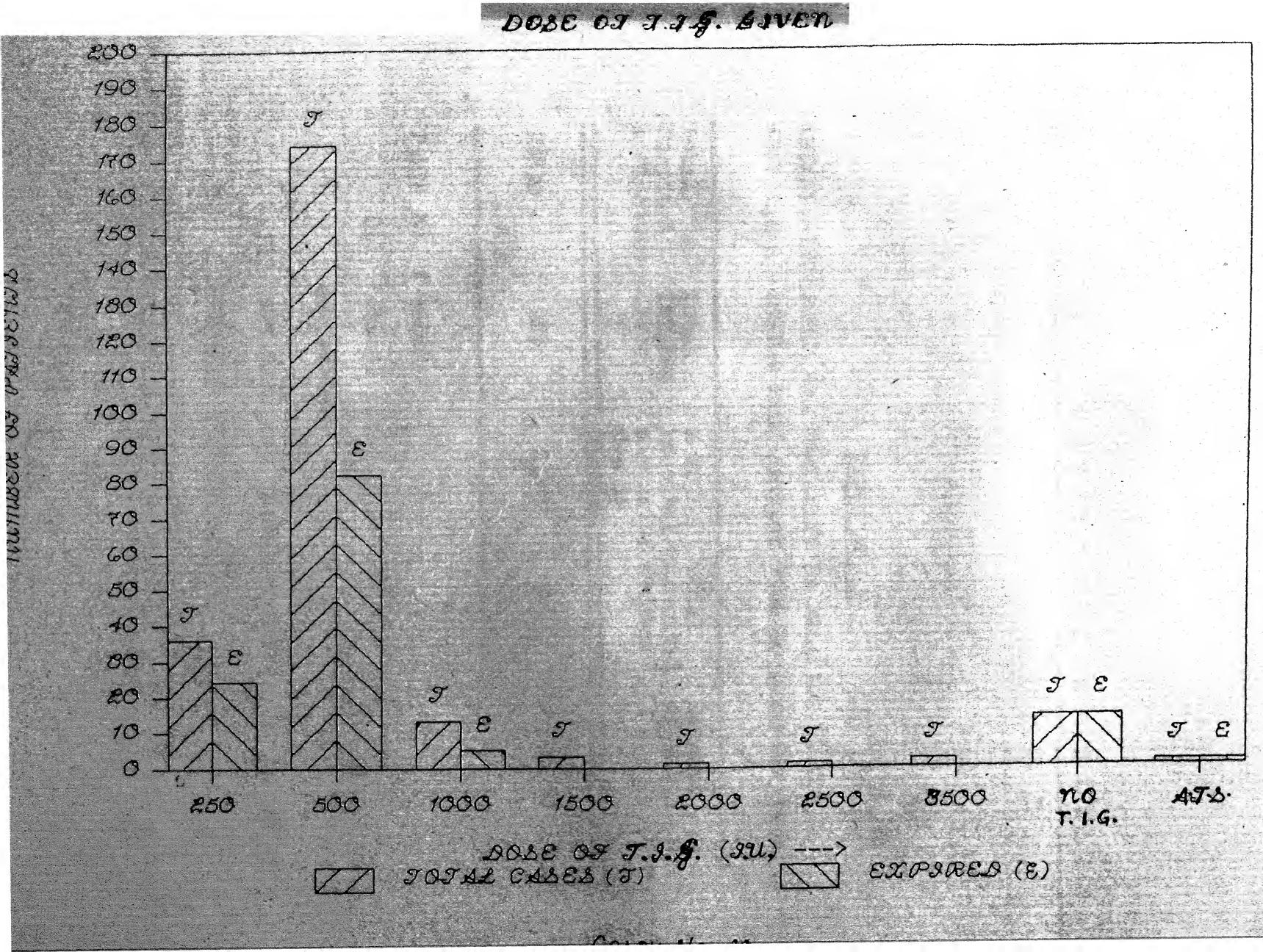

SEASONAL VARIATION (1988)
NUMBER OF PATIENTS
26
24
22
20
18
16
14
12
10
8
6
4
2
0
JAN
FEB
MAR
APR
MAY
JUN
JUL
AUG
SEP
OCT
NOV
DEC
MONTH --->
INCIDENCE
MORTALITY

Graph No. 9


SHOWING AGE AT DEATH / CURE
DEATH
+ CURE
NUMBER OF PATIENTS
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
AGE AT DEATH / CURE (Days)

graph no. 10

Graph No. 10 shows the age of neonate on admission in relation with mortality and survival. Most deaths in tetanus neonatorum cases occured between 4 to 11 days of age on admission. The maximum number of cases expired at the age of 6 days and 8 days on admission. Maximum number of neonates survived at the age of 11, 12 and 15 days on admission. Lesser the age, more were the chances of mortality.


DOSE OF T.I.G. GIVEN
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
NUMBER OF ANIMALS
T
E
250
500
1000
1500
2000
2500
3500
NO T.I.G.
ATS.
DOSE OF T.I.G. (IU.) --->
TOTAL CASES (T)
EXPIRED (E)

OBSERVATION TABLES

TABLE NO. 1

TETANUS-INCIDENCE AND MORTALITY IN RELATION TO TOTAL HOSPITAL ADMISSION FROM JANUARY 1988 TO DECEMBER 1988.

Total Hospital admissions	Total tetanus cases	% of hospital admission due to tetanus	Total Hospital deaths	Tetanus deaths	% of mortality due to tetanus
23530	285	1.21%	1452	126	8.67%

Table No. 1 shows -

(i) Tetanus cases comprised 1.21% of total hospital admissions.

(ii) Mortality due to tetanus was 8.67% of total hospital deaths.

TABLE NO. 2

INCIDENCE AND MORTALITY OF TETANUS IN THE DIFFERENT AGE GROUPS

Age group	No.of cases	% of total cases	No.of deaths	Mortality %
Adults	85	34.69%	36	42.35%
Neonates	82	33.47%	68	82.92%
Children	78	31.84%	22	28.20%
Total	245	100.00%	126	51.42%

Table No. 2 shows -

1. (i) Adult patients comprised 34.69% of total tetanus cases.
   (ii) Neonates comprised 33.47% of total tetanus cases.
   (iii)Children comprised 31.84% of total tetanus cases.

In the percentage contribution by the three groups adults contributed to higher number of cases (34.69%).

2. (i) Mortality in the adult group of patients was 42.35%.
   (ii) Mortality in the neonates was 82.92%.
   (iii)Mortality in children was 28.20%.

Mortality was highest in the neonatal group of patients (82.92%) and lowest in children (28.20%).

TABLE NO. 3

INCIDENCE OF TETANUS IN THE DIFFERENT AGE GROUPS ACCORDING TO SEX

Age group	Total cases	Males	%	Females	%	LAMA	Total study
Adult	90	49	54.44%	41	45.55%	5	85
Neonates	106	90	84.90%	16	15.09%	24	82
Children	89	58	65.16%	31	34.83%	11	78
Total	285	197	69.12%	88	30.88%	40	245

Table No. 3 shows the incidence of tetanus in the different age groups according to sex. It can be observed that tetanus is more common in males in all the age groups. This difference is the highest in neonates (84.90% of neonates were males).

TABLE NO. 4

TABLE SHOWING THE SEX RATIO OF PERCENT MORTALITY AND INCIDENCE IN THE DIFFERENT AGE GROUPS

Age group	Cases	M	F	M:F ratio	Mortality M	Mortality F	Ratio mortality % M	Ratio mortality % F	Mortality % M	Mortality % F
Adults	85	47	38	1.23:1	20	16	42.55%	42.10%	1.01:1	
Neonates	82	69	13	5.31:1	56	12	81.16%	92.31%		1:1.13
Children	78	54	24	2.25:1	13	9	24.07%	37.50%		1:1.56
Total	245	170	75	2.27:1	89	37	52.35%	49.33%	1.06:1	

Table No. 4 shows the sex ratio of percentage mortality and incidence in the different age groups. It can be seen that the male:female ratio is 2.27:1 which shows that tetanus is more common in males. The male:female ratio was the highest among neonates (5.31:1). Mortality was almost the same in both sexes, overall. However in children the mortality in female was 1.56 times that in males (M:F :: 1:1.56)

TABLE NO. 5

INCIDENCE AND MORTALITY OF TETANUS ACCORDING TO RURAL/URBAN AREAS

Age group	Total cases	Rural areas			Urban areas		
		Cases	Cases expired	% mortality	Cases	Cases expired	% mortality
Adults	85	79	33	41.77%	6	3	50.00%
Neonates	82	71	58	81.69%	11	10	90.90%
Children	78	74	21	28.37%	4	1	25.00%
Total	245	224	112		21	14	
Percentage		91.42%		50%	8.57%		66.66%

Table No. 5 shows -

(i) There is a much higher incidence of tetanus in the rural areas (91.42%) as compared to urban areas (8.57%).

(ii) Mortality is higher in patients from urban areas (66.66%) as compared to their rural counterparts (50%).

TABLE NO. 6

INCIDENCE AND MORTALITY ACCORDING TO SOCIO-ECONOMIC CONDITION

*Socio-economic group	Cases	% of total cases	Cases expired	% Mortality
Low	169	68.98%	101	59.76%
Middle	69	28.16%	23	32.33%
High	7	2.86%	2	28.57%
Total	245	100.00%	126	51.42%

* Socio-economic group

Low = Monthly income ⟨ Rs. 500/-

Middle = Monthly income between Rs 500/- to 1000/-

High = Monthly income ⟩ Rs 1000/-

Table No. 6 indicates -

(i) Patients of low socio-economic group contribute to the highest incidence of tetanus (68.98%) amongst all groups. Mortality was also the highest in this group (59.76%).

(ii) The lowest incidence was found in the high socio-economic group (2.86%) amongst all groups. Mortality was the lowest in this group (28.57%).

TABLE NO. 7

INCIDENCE AND MORTALITY OF TETANUS ACCORDING TO OCCUPATION

Occupation	No.of patients	Cases expired	% mortality
1) Rural student	52	14	26.92%
2) Labourer/farmer	48	20	41.66%
3) Businessman	3	1	33.33%
4) Housewife	29	12	41.37%
5) Cobbler	1	1	100.00%
6) Shepherd	1	1	100.00%
7) Dairy business	1	0	0.00%
8) Potter	1	1	100.00%
9) Clerk	1	0	0.00%

Table No. 7 shows the incidence and mortality of tetanus in relation to occupation. It can be observed that the incidence of tetanus was the highest in rural based students/ children (52 patients). It was followed by labourer/farmers (48 patients). It was common in housewives also (29 patients). The mortality was the highst in a cobbler, a shephered and a potter(100%). It was followed by farmer/labourers, and housewives (41.66% and 41.37% respectively).

It was lower in businessmen (33.33%) and clerks.

TABLE NO. 8

INCIDENCE AND MORTALITY IN RELATION TO ETIOLOGICAL FACTORS

Mode of infection	No.of cases	% of total cases	No.of deaths	% Mortality
Traumatic	50	20.41%	22	44%
Otogenic	24	9.79%	8	33.33%
Wire/nail prick	10	4.08%	4	40%
Thorn prick	8	3.26%	1	12.50%
Post partum tetanus	6	2.45%	3	50%
Post measles tetanus	1	0.41%	0	0%
Post mumps tetanus	1	0.41%	0	0%
Boil/furunculosis	4	1.63%	2	50%
Post M.T.P./ligation	1	0.41%	0	0%
Post burn	2	0.81%	2	100%
Following infection	2	0.81%	0	0%
Following biopsy	1	0.41%	0	0%
Tooth extraction	1	0.41%	0	0%
Gunshot wound	2	0.81%	0	0%
Oro-pharyngeal infection	4	1.63%	0	0%
Folbwing tongue bite	1	0.41%	0	0%
Pharyngeal carcinoma	1	0.41%	0	0%
Ectopia vesicae	1	LAMA	LAMA	LAMA
Post goat bite	1	0.41%	0	0%
Not known	42	17.14%	16	38.09%
	163		58	
Tetanus neonatorum	82	33.46%	68	82.92%
Total	245	100%	126	51.42%

Etiological factors

Table No. 8 shows the various etiological factors and their relation to mortality. It is seen that trauma was the commonest cause of tetanus in adults and children (20.41%) and otogenic infection the next common etiological factor (9.79%). Wire/nail/thorn prick, post partum infection, boils, burns, injections, oropharyngeal infections, gun shot wound, measles, mumps, biopsy, tooth extraction, MTP/ligation and goat bite were the other etiological factors. There was one case of adult tetanus folbwing carcinoma of pharynx and another unusual case, of tetanus in a child with ectopia vesicae. In 17.14% of patients (excluding neonates) the etiological factor or the site of entry of tetanus bacilli could not be determined.

The mortality was highest in tetanus following burns (100%). It was followed by post partum tetanus (50%), tetanus following boils (50%), post traumatic tetanus (44%) and tetanus following wire/nail pnick (40%). The mortality was lower in tetanus following otogenic infections (33.33%), followed by tetanus due to thorn prick (12.5%). It was zero in tetanus due to all other causes mentioned above.

In tetanus cases where the etiological factor was unknown the mortality was on the higher side (38.09%).

TABLE NO. 9

TABLE SHOWING NEONATAL TETANUS MORTALITY IN DIFFERENT CENTRES

Authors	Place	% mortality
1) Patel and Mehta	Bombay	86.4%
2) Bhatt and Anwikar	Bombay	86.0%
3) Armegnaud and Ray	Dakar	91.92%
4) Present study	Jhansi (Bundelkhand)	82.92%

TABLE NO. 10

TETANUS NEONATORUM- TABLE SHOWING MATERIALS APPLIED ON THE UMBILICAL CORD

Materials applied	No.of cases	Percentage
Mustard oil	25	30.49%
Groundnut oil	3	3.66%
Ash	8	9.75%
Powder	5	6.09%
Paint	2	2.43%
Spirit	1	1.22%
No application	38	46.34%
Total	82	100%

Table No. 10 shows that mustard oil was the most commonly used application on umbilical cord (applied on 30.49% of neonates). Ash was another commonly used application (9.75%) of cases. However no application was used in 46.34% of neonates.

TABLE NO. 11

TABLE SHOWING INSTRUMENTS USED FOR CUTTING THE UMBILICAL CORD IN TETANUS NEONATORUM CASES

Instrument used	No. of cases	Percentage
Home delivery		
Shaving blade	73	89.02%
Knife/Sickle	9	10.98%
Hospital delivery	0	0
Total	82	100%

Table No. 11 shows that unsterile shaving blade was the most commonly used instrument for cutting the umbilical cord (in 89.02% of tetanus neonatorum cases). All patients (Neonates) were delivered at home by untrained dais mostly or by an elderly lady of the house.

TABLE NO. 12

PROGNOSIS IN RELATION TO DURATION OF SYMPTOMS BEFORE ADMISSION

Duration of symptoms before admission (days)	No.of cases	% of total cases	No.of deaths	% mortality
Upto 1 day	75	30.62%	55	73.33%
2 days	59	24.08%	36	61.01%
3 days	44	17.96%	18	40.91%
4 days	18	7.34%	6	33.33%
5 days	16	6.53%	5	31.25%
6 days	13	5.31%	2	15.38%
7 days	3	1.22%	0	0.0%
8 days	5	2.04%	1	20.00%
more than 8 days	12	4.90%	3	25.00%
Total	245	100.00%	126	51.42%

Table No. 12 gives the duration of symptoms before admission and its relation to prognosis. It is seen that the shorter the duration of symptoms before admission, the higher was the mortality. The mortality was the highest when the duration of symptoms was less than or equal to one day (73.33%). It steadily decreased to zero when the duration of symptoms was 7 days. However there was a slight rise in mortality (20%)when the duration of symptoms was more than 7 days.

It was observed that lock jaw, neck rigidity, dysphagia and convulsions were the usual presenting features in adults and children. Neonates manifested with excessive crying, refusal/inability to suck, besides convulsions.

TABLE NO. 13

MORTALITY IN RELATION TO GRADES OF SEVERITY

Grades	Total cases	Cases expired	Percentage of mortality
I	4	0	0
II	42	4	9.52%
III	36	5	13.88%
IV	76	42	55.26%
V	87	75	86.20%
Total	245	126	51.42%

Table No. 13 shows the mortality due to tetanus according to the grade of severity of tetanus. It can be seen that the mortality was the lowest (zero) in grade I patients. The mortality increased from 9.52% in grade II to 86.20% in grade V patients. Thus mortality increases with increasing grades of severity of tetanus.

TABLE NO. 14

PROGNOSIS IN RELATION TO INCUBATION PERIOD

Incubation period (days)	No. of cases	% of total cases	No. of deaths	% mortality
0-7 days	115	46.94%	81	70.43%
8-14 days	61	24.89%	20	32.78%
15-21 days	7	2.86%	2	28.57%
7 21 days	8	3.26%	1	12.50%
Not known	54	22.05%	22	40.74%
Total	245	100.00%	126	51.42%

Table No. 14 gives the relation of incubation period to prognosis. It is seen that the mortality was maximum when the incubation period was less than 7 days (70.43%) and was least when the incubation period was more than 21 days (12.5%). Where the incubation period was unknown the mortality was high (40.74%).

TABLE NO. 15

PROGNOSIS IN RELATION TO PERIOD OF ONSET

Period of onset (hours)	No.of cases	% of total cases	No.of deaths	% of mortality
=or / 24 hours	136	55.51%	104	76.47%
25 - 48 hours	44	17.96%	13	29.54%
49 - 72 hours	16	6.53%	4	25.00%
7 72 hours	13	5.31%	2	15.38%
No period of onset present (spasms absent)	36	14.69%	3	8.33%
Total	245	100.00%	126	51.42%

Table No. 15 shows the prognosis in relation to period of onset. As seen from this table spasms (convulsions) were absent in 14.69% cases. Mortality was lowest in this group (8.33%). The mortality was the highest when the period of onset was less than 24 hours (76.47%) and it steadily decreased to 15.38% when the period of onset was more than 72 hours.

TABLE NO. 16

PROGNOSIS IN RELATION TO TEMPERATURE ON ADMISSION

Temperature renge	No.of cases	% of total cases	No.of deaths	% mortality
∠ 99°F	67	27.35%	9	13.43%
99°F - 100°F	129	52.65%	79	61.24%
7 100°F	49	20.00%	38	77.55%
Total	245	100.00%	126	51.42%

Table No. 16 gives the severity of fever at the time of admission and its relation to mortality. It is seen that the mortality was minimum when the temperature was below 99°F (13.43%). The mortality increased to 77.55% when the temperature was more than 100°F.

TABLE NO. 17

RISUS SARDONICUS AND ITS RELATION TO MORTALITY

* Severity of risus	No.of cases	% of total cases	No.of deaths	Mortality %
Risus absent	17	6.94%	2	11.76%
Mild	55	22.45%	9	16.36%
Moderate	44	17.96%	17	38.63%
Severe	129	52.65%	98	75.97%
Total	245	100.00%	126	51.42%

* Grading of severity of Risus was as follows

Mild = Furrows seen on forehead during spasms and absent when patient was sedated.

Moderate = Furrows on forehead seen more prominently on spasms.

Severe = Prominent furrows which could be seen at any time.

Table No. 17 shows the prognosis in relation to the severity of risus. It can be seen that mortality was lowest (11.76%) when risus was absent. It was 16.36% in cases with mild risus and the mortality increased to 75.97% in cases with severe risus. It was also observed that risus was one of the last symptoms to disappear.

TABLE No. 18

NECK RIGIDITY AND ITS RELATION TO MORTALITY

*Grade	No.of cases	% of total cases	No.of deaths	Mortality %
Absent	7	2.85%	2	28.57%
Mild	58	23.67%	12	20.68%
Moderate	101	41.23%	44	43.56%
Severe	79	32.25%	68	86.08%
Total	245	100.00%	126	51.42%

* Grading of Neck Rigidity was done as follows

Mild = Chin approximation with chest possible with difficulty.

Moderate = Only slight bending possible.

Severe = No movement possible.

Table No. 18 shows the severity of neck rigidity and its relation to prognosis. It is seen that mortality increased from 20.68% in cases of mild neck rigidity to 86.08% in cases with severe neck rigidity. The mortality was 28.57% in cases without any neck rigidity. It was also one of the last symptoms to disappear.

TABLE NO. 19

RELATION OF SEVERITY OF DYSPHAGIA TO PROGNOSIS

*Grade	No.of cases	% of total cases	No.of deaths	Mortality %
Absent	9	3.67%	0	0
Mild	55	22.45%	4	7.27%
Moderate	69	28.16%	25	36.23%
Severe	112	45.72%	97	86.60%
Total	245	100.00%	126	51.42%

* Severity of dysphagia was classified as follows

1) Mild - can swallow liquids easily.

2) Moderate - can swallow few drops only.

3) Severe - can swallow few drops with difficulty or becomes asphyxiated on swallowing fluids.

Table No. 19 shows the severity of dysphagia and its relation to prognosis. It is seen that the mortality increased from 7.27% in cases of mild dysphagia to 86.60% in cases with severe dysphagia. In patients without any dysphagia mortality was zero.

TABLE NO. 20

RELATION OF SEVERITY OF LOCK JAW TO MORTALITY

Grade*	No.of cases	% of total cases	No.of deaths	Mortality %
Absent	5	2.04%	0	0
Mild	57	23.26%	8	14.03%
Moderate	99	40.42%	46	46.46%
Severe	84	34.28%	72	85.71%
Total	245	100.00%	126	51.42%

* Lock Jaw was graded as follows

Mild - Mouth opening present but not full.

Moderate - Slight mouth opening present with difficulty.

Severe - No mouth opening present.

Table No. 20 shows the relation of severity of lock jaw to prognosis. It can be seen that lock jaw was mild to moderate in about 64% of cases. Mortality increased from 14.03% in cases with mild lock jaw to 85.71% in severe lock jaw cases.

TABLE NO. 21

PROGNOSIS IN RELATION TO SEVERITY OF SPASMS

Grade	No.of cases	% of total cases	No.of deaths	% Mortality
Mild	45	18.38%	6	13.33%
Moderate	49	20.00%	20	40.82%
Severe	121	49.38%	98	80.99%
No spasms	30	12.24%	2	6.66%
Total	245	100.00%	126	51.42%

Table No. 21 shows the prognosis in relation to the severity of spasms (convulsions). 12.24% of patients had no spasms. The mortality in this group was the lowest (6.66%). In patients with mild spasms the mortality was 13.33%. When spasms were severe the mortality increased to 80.99%.

TABLE NO. 22

MORTALITY IN RELATION TO DAY OF ADMINISTRATION OF T.I.G.

Day of administration	Total cases	Cases expired	% Mortality
Ist day	212	97	45.75%
IInd day	15	11	73.33%
IIIrd day or beyond	4	4	100.00%
T.I.G. not given	14	14	100.00%
Total	245	126	51.42%

Table No. 22 shows the effect of delay in the administration of T.I.G. on the mortality. It can be seen, that mortality was the lowest, when the patients were administered T.I.G. on the same day of admission (45.75%). The mortality shot up to 73.33%, when T.I.G. was given on the second day. Mortality was 100% when T.I.G. was administered on/beyond the third day. This goes to prove that T.I.G. needs to be administered immediately, on admission of the patient in order to be effective.

TABLE NO. 23

MORTALITY ACCORDING TO ROUTE OF ADMINISTRATION OF T.I.G.

Age group	Intrathecal T.I.G.			Intramuscular T.I.G.		
	Cases	Cases expired	% mortality	Cases	Cases expired	% mortality
Adults	72	27	37.5%	8	7	87.5%
Children	70	18	25.7%	4	3	75.0%
Neonates	72	52	72.2%	5	5	100.0%
Total	214	97	45.32%	17	15	88.23%

Table No. 23 shows the mortality according to the route of administration of T.I.G. in the different age groups. It can be obs-erved that patients who received intrathecal T.I.G. had a lower mortality as compared to those who received intramuscularly in all age groups. Mortality was the lowest in children (25.7%) who received intrathecal T.I.G. as compared to those who received intramuscularly (75%).

TABLE NO. 24

MORTALITY IN THE DIFFERENT GRADES OF TETANUS IN RELATION TO ROUTE OF ADMINISTRATION OF T.I.G.

Grades	Intrathecal T.I.G.			Intramuscular T.I.G.		
	Cases	Expired	% mortality	Cases	Expired	% mortality
I	4	0	0	0	0	0
II	38	2	5.26%	1	1	100%
III	33	3	9.09%	1	0	0%
IV	65	31	47.69%	4	3	75%
V	74	61	82.43%	11	11	100%

Table No. 24 shows the mortality in the different grades of tetanus, in relation to the route of administration of T.I.G. It can be seen that the mortality was only 5.26%, when T.I.G. was given intrathecally in grade II patients, as compared to 100% mortality in the same grade, when T.I.G. was given intramuscularly. In grade IV patients the mortality was 47.69% when given intrathecally and 75% when given intramuscularly. Mortality was high in grade V patients even when T.I.G. was administered intrathecally (82.43%), although it was lower as compared to the intramuscular group in the same grade (100%). It can be inferred that the effectiveness of T.I.G. is better, when administered intrathecally in all grades of tetanus, although it appears to be more effective in the milder grades of tetanus.

TABLE NO. 25

MORTALITY IN RELATION TO DOSE OF T.I.G. ADMINISTERED

Dose of T.I.G.	Total cases	Cases expired	Percentage mortality
250 I.U.	36	24	66.66%
500 I.U.	174	82	47.12%
1000 I.U.	13	5	38.46%
1500 I.U.	3	0	0%
2000 I.U.	1	0	0%
2500 I.U.	1	0	0%
3500 I.U.	2	0	0%
No T.I.G. or A.T.S. given	14	14	100%
Only A.T.S. given (20,000 units)	1	1	100%
Total	245	126	51.42%

Table No. 25 shows tetenus mortality in relation to the dose of T.I.G. given. That with a dose of 250 I.U. of T.I.G., the mortality was high (66.66%). With a dose of 500 I.U. of T.I.G. it declined to 47.12%. With doses of 1000 I.U. and above it declined to zero when the range of the dose of T.I.G. given was 1500 I.U. to 3500 I.U. Mortality was 100% when no T.I.G. or A.T.S. was given. 1 patient received A.T.S. only but he expired. It can be thus seen that higher doses of T.I.G. are beneficial in lowering mortality due to tetanus.

TABLE NO. 26

ASSUMED CAUSES/COMPLICATIONS CONTRIBUTING TO DEATH

Complications	No.of deaths	% of mortality
Respiratory spasm leading to severe apnoeic spells	56	44.46%
Pulmonary complications (including infections)	27	21.43%
Uncontrolled septicemia	3	2.38%
Renal complications	3	2.38%
Toxemia of gangrene	1	0.79%
Jaundice	1	0.79%
Oversedation	10	7.93%
*Facial palsy	0	0
Not known	25	19.84%
Total	126	100.00%

* 1 patient developed residual facial palsy but he improved.

Table No. 26 shows that respiratory spasm leading to severe apnoeic spells was the probably cause in 44.46% of total deaths.

Pulmonary complications including acute secondary lung infections top-ped the list of complications contributing to 21.43% of all deaths. 3 patients died of uncontrolled septicemia (2.38% of all deaths). 3 patients died of renal complications including renal failure (2.38% of all deaths). One patient died of toxemia due to gangrene.

Oversedation contributed to 7.93% of all deaths, while in 19.84% of deaths the exact cause was not known.

Photograph of a case of post-partum tetanus, showing, severe risus sardonicus, severe neck rigidity and severe lock jaw.

Photograph showing a case of tetanus neonatorum, having a convulsive episode. The neonate also shows, severe neck and limb rigidity, opisthotonous and risus sardonicus.

Photograph of a tetanus patient with severe opisthotonous and limb rigidity.

Photograph showing a case of childhood tetanus, with risus, neck rigidity and mild lock jaw.

Photo showing the two varieties of T.I.G. used in the present study. (i.e. 500 I.U. vial with diluent and 250 I.U. ampoule).

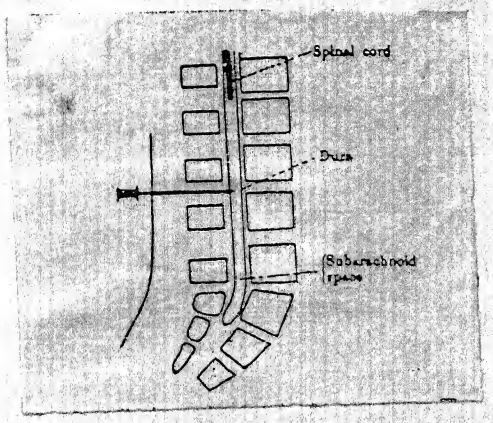


Diagram showing the route of needle in performing lumbar puncture for intrathecal administration of T.I.G.

DISCUSSION

D I S C U S S I O N

Tetanus is still a formidable problem in our country and carries a high mortality. The treatment of tetanus has been mainly symptomatic. An expanding list of drugs used to achieve symptomatic control, only show that none of the drugs evolved so far satisfies the criteria of an ideal drug. Tetanus is almost unique among the bacterial diseases in having so far defied all therapeutic agents directed against it (Vaishnava et al, 1966). Although human antitetanus immunoglobulin (T.I.G.) has been available in the recent years, its role is yet to be determined and the method of administration and dosage has yet to be standardized.

In the present study from January 1988 to December 1988, tetanus cases comprised of 1.21% of total hospital admissions. Most of the patients were from Jhansi district of Bundelkhand region, followed by Shivpuri, Tikamgarh, Jalaun, Hamirpur, Datia, Lalitpur, Gwalior and Bhind districts of the Bundelkhand region. Illiteracy, poverty, lack of immunisation and poor medical facilities in the periphery, unhygienic customs and delivery practices are all rampant in this region although Bundelkhand has a rich historical and cultural background. This is one of the reasons for such a high

incidence of tetanus in the aforesaid areas. It is also possible that the soil in these regions especially in Jhansi region is more enriched with Clostridium tetani.

As regards tetanus cases in relation to total hospital admissions, Laha and Vaishya (1963) reported 4.8% cases due to tetanus. In the present study tetanus cases were 1.21% of total hospital admissions. Tetanus deaths in the present study accounted for 8.67% of total hospital deaths. Vaishnava et al (1966) reported 16% of total hospital deaths due to tetanus.

The comparetive figures of the year 1983 and 1988 show an increased incidence and decreased mortality of tetanus in 1988 (Overall mortality was 68.53% in 1983 as compared to 51.42% in 1988) Better survival in 1988 may be attributed to the use of intratheeal T.I. G. in 1988(as compared to A.T.S. only in 1983).

Most tetanus deaths occurred within the first week of admission, the maximum deaths occurring on the Ist and 2nd days following admission. Vaishnava et al (1966) noted somewhat similar observations. Though the patients started to improve from the 2nd day onwards maximum care occurred between 6th and 9th days. After that it remained constant till the seventeenth day.

Overall tetanus mortality in the present study was 51.42%. Adults had a higher incidence of tetanus among all groups (34.69% of total cases). The maximum mortality was found in tetanus neonatorum cases (82.92%). Lowest mortality was observed in the children (28.20%). Patel (1965) reported a mortality of 86.5% in tetanus neonatorum. Phatak et al (1973), reported 87.80% mortality in neonatal tetanus. Athavale et al also found a high mortality in neonatal tetanus. Sehgal et al reported an overall mortality of 86.2% in neonates, Childhood tetanus constituted 31.84% of total cases. Athavale et al, reported in their series an incidence of 39% of total cases due to childhood tetanus.

There was also, a high overall incidence of tetanus neonatorum (33.47%) in our present study. Bhat et al reported an overall incidence of 14.3% of tetanus neonatorum. Suri (1966), reported 26.8% overall incidence of tetanus neonatorum.

As adults were more prone to injuries and infections (they more active physically) there was a slightly higher incidence of tetanus in this group. Also, women in this age group, contributed to the child bearing age and were thus susceptible to puerperal tetanus. Domiciliary deliveries by untrained midwives (dais) and

the use of unsterile materials for cord cutting and dressing (mustard oil, ash, etc.), all performed under unhygienic conditions, made the neonates very susceptible to tetanus. Bollet and Punjabi (1964) observed 100% home deliveries in neonatal tetanus.

The high mortality in the neonates can be explained by the reason, that on entry of the Clostridium tetani spores, in the infants umbilical cord, the exotoxins subsequently released are quantitatively the same as in adults (Khanna S.S. et al).

Childhood tetanus contributed to the least overall tetanus mortality, which proves that children could withstand the disease better. La force (1965) pointed high case fatality rates in tetanus in the extremes of age group.

The overall male/female ratio was 2.27:1 in the present series. This ratio was the highest in neonates (M:F :: 5.3:1). Mortality ratio of male:female was overall 1.06:1. It can be thus seen that the incidence was higher in males whereas tetanus mortality was nearly the same in both sexes. Mathur (1980) reported a male/female ratio of 5.4:1, in tetanus. Kacharevic suggested that males were more sensitive to tetanus toxin as compared to females and hence a higher male preponderance. Suri et al, found that tetanus mortality in the two sexes did not

In the present study most of the cases of tetanus were from rural areas (91.42% of all cases). Patients drawn from rural areas were mostly labourer/ farmers (i.e. they were engaged more in manual work and were more exposed to Clostridium tetani infection from soil etc. while handling). Thus a higher incidence was observed in patients from rural areas. On the other hand, because of lack of proper medical care and facilities in rural areas, such patients rushed to our hospital as soon as symptoms appeared and treatment could be started earlier (hence a lower mortality of rural tetanus patients 50%). On the contrary urban patients tried household remedies and took the help of local quacks, before they came to the hospital, though the access to the later was easier for them; consequently there was a higher mortality (66.06%) in them.

A higher incidence of tetanus neonatorum was found between June and November, although it was most prevalent during the monsoon season, in our present study. An increased birth rate during this season may be the possible reason for this (Guha, Mazumdar and Chakraborty, 1974).

Bhat et al (1979) noted a higher incidence of tetanus neonatorum between June and October. Vaishnava et al, also noted a higher incidence during the monsoon

period. In the present study the peak incidence of childhood tetanus was found in March and April months. The posible explanation to this, is that children mostly stayed outdoors during this period.

The incidence of tetanus was the highest in the low socio-economic group of patients (68.98%) and the lowest in the high socio-economic group of patients (2.86%). The highest mortality was noted in the low socio-economic group of patients (59.76%) and the lowest in the high income group (28.59%). Higher incidence and mortality in the low socio-economic group patients can be attributed to the reason, that such patients on account of poverty & illiteracy were more nutritionally deprived, had a lower immunity, were more exposed to manual labour and more used to unhygienic customs and practices.

Rural children/students, labourer/farmers were all, more exposed to trauma and subsequent infections and therefore had a higher incidence of tetanus. Mortality was also high in such patients. However the highest mortality was observed in a cobbler, shepherd and a potter. It can be observed that all were manual labourers. In the cobbler the infection source was probably from handling footwear (leather material) besides handling old contaminated footwear for repair purposes.

Shepherds have a closer contact with sheep and cattle. Moreover they usually walk barefooted while rearing cattle. It would be expected that they are more prone to tetanus under such conditions.

Potters are engaged in handling clay with hands minor abrasions on the hand lead to ideal situations for Clostridial proliferation.

Post partum and post abortal tetanus had a high mortality (50%). Post-partum uterus provides a good anaerobic environment for Clostridial proliferation and this could be the possible explanation for puerperal tetanus. Shah et al (1962) found 59% mortality in post-partum tetanus.

Trauma was the most common etiological factor (20.41%). Otogenic infection was the next common etiological factor (9.79%), especially so in children, besides trauma. In an equally large number of cases (17.14%) no obvious cause could be found. Wesley et al, noted that tetanus was more common in bare-footed children who had no obvious injury.

Lock jaw, neck rigidity and dysphagia were the most common early complaints in all patients. In neonates it was excessive crying and inability to suck. Convulsions

appeared sooner in neonates. Most deaths in tetanus neonatorum cases occurred between 4 to 11 days of age at admission. Lesser was the age of the neonate at admission, the more was the mortality. Maximum recoveries in tetanus neonatorum cases occurred between the ages of 11 and 15 days on admission. Sokal et al, pointed that most deaths in neonatal tetanus patients, occurred at 4 to 14 days on admission. Phatak et al, noted that no neonate of or below the age of 7 days, on admission survived. He also observed that maximum number of neonates survived at an average age of 10.6 days on admission.

It was observed in the present study that shorter the duration of symptoms were, before admission the higher was the mortality. The mortality was the highest (73.33%) when the duration of symptoms on admission was approximately 1 day. Phatak et al. noted that the disease pursued a milder course in neonates, who came to the hospital late after the onset of the disease. Athavale et al, observed that prognosis was worse in patients with a shorter duration of symptoms on admission, in children and neonates.

In the present series, it was observed that mortality increased with increasing grades of severity of tetanus on admission. This was in accordance with the Patel &

Joag's system of grading tetanus severity. Athavale et al, Jolly et al, also found similar observations. It was observed that mortality increased with a shorter incubation period, whereas a longer incubation period was associated with a better prognosis. (When incubation period was less than 7 days mortality was 70.43% and when more than 21 days it was 12.5%). Jolly et al, Vaishnava et al, have all noted that prognosis varies directly with the incubation period.

Where the period of onset was absent, the mortality in such patients was the lowest (8.33%). Mortality was the highest when the period of onset was less than 24 hours (76.47%). A shorter period of onset was associated with a worse prognosis. Cole, first reported that period of onset modified the outcome of the disease. Athavale et al, Bhat et al, Phatak et al, have all noted similar observations.

Mortality due to tetanus increased with temperature on admission (or within 24 hours of admission). With temperatures below 99°F it was 61.24% and with temperatures beyond 100°F the mortality was 77.55%. Spaeth et al, Vaishnava et al, Athavale et al, have all reported fever as a bad prognostic factor.

It was also found that prognosis was directly related to the severity of risus on admission. Mortality in patients with mild risus was 16.36%. It shot up to 75.97% in patients with severe risus. Risus was one of the last symptoms to disappear. Athavale et al, also noted similar observations.

Mortality was found to increase with increasing severity of neck rigidity on admission. Also, it was one of the last symptoms to disappear. Vaishnava et al, found that mortality increased with increasing severity of rigidity.

In the present study it was observed that increasing severity of dysphagia was associated with a worse prognosis. Mortality was 7.27% in tetanus patients with mild dysphagia. It increased to 86.60% in patients with severe dysphagia. Athavale et al, noted in children that mortality increased from 9.1% in cases with mild dysphagia to 100% in cases with very severe dysphagia. In neonates also he observed that mortality increased with severe grades of dysphagia. Phatak et al, have suggested that lock jaw and dysphagia increase the risk of aspiration pneumonia and consequently increased mortality.

It was observed that mortality increased with increasing severity of lock jaw in tetanus patients (mortality in mild lock jaw cases was 14.03% and 85.71% in severe cases). Athavale et al, also found an increase in mortality with increase in severity of lock jaw. Vaishnava et al, Bhandari et al, have also noted similar observations.

Spasms (convulsions) were one of the most important factors with regards to prognosis. It was found that mortality increased from 13.33% in patients with mild spasms to 30.99% in patients with severe spasms. Mortality thus increased with increase in the severity of spasms. Vaishnava et al, Bhat et al, Bhandari et al, all noted a similar finding.

Therapy

Fortunately nowadays with the availability of human tetanus immunoglobulin, tetanus treatment has become safer as compared to, in the past and even in the present times with the use of A.T.S.(equine). The present trial was done to assess the efficacy and the results of intrathecal administration of human anti-tetanus immunoglobulin (T.I.G.).

It was observed that overall mortality increased from 45.75% in patients receiving T.I.G. on the same day of admission to 100% in cases who received T.I.G.

on or after the IIIrd day of admission. This goes to prove that in order to be effective, T.I.G. should be given as early as possible on admission. Keswani et al, noted that with intrathecal administration of A.T.S. there was a mortality of 21.05% when the delay in administration of A.T.S. was upto 24 hours. Mortality increased substantially with further delay over 48 hours. Sanders et al, postulated that free toxin is available for neutralisation by intrathecal administration of tetanus antitoxin which circumvents the blood brain barrier. But probably after 48 hours, when the toxin is presumed to be fixed to the nervous tissue, intrathecal tetanus antitoxin is not of much value.

It was observed that intrathecal T.I.G. was more effective in all grades of severity of tetanus as compared to intramuscular T.I.G. In grade II patients mortality with intrathecal T.I.G. was 5.26% as compared to 100% mortality with intramuscular T.I.G. Similarly in grade IV cases mortality with intrathecal T.I.G. was 47.69% as compared to 75% mortality with intramuscular T.I.G., in the same grade. It was seen that intrathecal T.I.G. was more useful in milder cases of tetanus. Gupta P.S. et al (1980), also found similar observations with intrathecal T.I.G. In his series tetanus mortality was reduced to

2.04% with intrathecal T.I.G., from 21% with intramuscular T.I.G., in patients with mild tetanus, when administered early in the disease. Intrathecal T.I.G. was better in all grades of severity of tetanus, although its efficacy decreased with increasing severity of tetanus, in our series.

With the use of intrathecal T.I.G. in 72 adults, 70 children and 72 neonates, mortality was 37.5%, 25.7% and 72.2% respectively, as compared to a mortality of 87.5%, 75.0% and 100.00% respectively on using intramuscular T.I.G. in the same groups. Thus intrathecal T.I.G. was most effective in children.

Higher doses of T.I.G. were more effective in lowering tetanus mortality. The mortality was 66.66% with a dose of 250 I.U. of T.I.G., 47.12% with a dose of 500 I.U., 38.46% with a dose of 1000 I.U. and zero with doses of 1500 I.U. to 3500 I.U. Unfortunately only 7 patients could afford doses of 1500 I.U. and above owing to the high costs of T.I.G. However, it can be safely concluded that a minimum of 500 I.U. to 1000 I.U. of T.I.G. is essential by intrathecal route for tetanus therapy. It would be ideal if doses above 1500 I.U. could be given intrathecally. Chopra et al (1986) also found a beneficial effect of intrathecal T.I.G. in high doses in

moderate and severe cases of tetanus. On the contrary Vakil et al (1977), Chugh et al (1955), found no beneficial effect of T.I.G.

Intramuscular T.I.G. was only administered in such patients where intrathecal procedure failed.

Better results of intrathecal T.I.G. are probably becuase of the direct action of T.I.G. on the unfixed circulating toxins in the central nervous system in C.S.F., by their neutralisation.

Intrathecal administration of T.I.G.needs to performed with care, owing to the risk of tonsillar herniation, as C.S.F. tension is increased in tetanus. However, no complications were noted due to intrathecal instillation of T.I.G., either because of the procedure or because of the drug itself. T.I.G. was found to be safe and free from any side effects.The intrathecal route was superior.

In the present study 3 patients expired due to renal complications. Venkat Raman et al, also have reported renal failure in tetanus.

Pulmonary complications including acute secondary lung infections was the most commonly assumed complication. Unfortunately no attendant submitted his patient for

autopsy. So the exact morbid pathology of cause/complications leading to death couldnot be determined. Most patients at the time of death suffered from severe respiratory spasms with apnoeic spells. Tracheostomy was performed in 5 patients but none survived.

The incidence of tetanus in Bundelkhand continues to be high, owing to the fact that even after so many years of independence thés region continues to be socio-economically backward. Consequently illiteracy and poverty are rampent, as is the lack of medical care infrastructure. Proper health planning and management are essential in order to provide adequate protection from tetanus and so many other diseases. Immunization and maternal and child health services need greater attention, alongwith provisions for adequate medical care and education, so that the disease may be arrested early and be possibly eradicated by universal immunization.

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CONCLUSION

CONCLUSIONS

The following conclusions were drawn from the present study:

1. Jhansi (U.P.) contributed to the highest number of tetanus cases (148 cases) from the Bundelkhand region, in this hospital. Shivpuri and Tikamgarh (M.P.) contributed to 34 and 32 cases respectively after Jhansi. Cases also came from Jalaun (U.P.), Hamirpur (U.P.), Datia (M.P.), Lalitpur (U.P.), Gwalior (M.P.), Bhind (M.P.) and Sagar, in that order.
2. Tetanus cases comprised of 1.21% of total hospital admissions in M.L.B. Medical College, Hospital, Jhansi (U.P.) from January 1988 to December, 1988. Tetanus deaths accounted for 8.67% of total hospital deaths.
3. Most tetanus deaths occurred within the first week of admission, the peak incidence of deaths being on the Ist and 2nd days of admission. Maximum recovery of the patients occurred between the 6th and 9th days of admission, remaining nearly constant till the seventeenth day. Late deaths probably due to secondary complications occurred after the 13th day of admission.
4. Out of the total tetanus patients admitted, adults had the highest incidence (34.69%) and the children, the lowest (31.84%). Neonates contributed to 33.47% of

The highest mortality was found in neonatal tetanus (82.92%) and the lowest in childhood tetanus cases (28.20%). Adults had a mortality of 42.35% due to tetanus.

5. The incidence of tetanus was more common in males in all the age groups (197 male cases as compared to 88 female cases in total). Among neonates the male:female ratio was the highest (5.31:1). The overall male:female ratio was 2.27:1. Mortality was nearly the same in both sexes. (M:F :: 1.06:1) though female children had a slightly higher mortality (M:F :: 1:1.56).
6. Urban areas contributed to a lower incidence of tetanus (8.57%) and a higher mortality (66.06%) whereas rural areas contributed to a higher incidence (91.42%) and a lower mortality (50%).
7. In neonates and children there was a definite seasonal variation. Tetanus neonatorum was most prevalent during the monsoon season. In children the incidence was highest in summer months. In children there was also a high incidence during the winter months (September to December).
8. The incidence and mortality of tetanus were the highest in the low socio-economic group of patients (68.98% and 59.76% respectively).

9. There was a higher incidence of tetanus among rural students/children, labourer/farmers and housewives. Mortality was high in a cobbler, shepherd and a potter (100% each), labourers (41.66%) and housewives (41.37%).

10. Trauma was the commonest cause of tetanus in adults and children (20.41%) followed by otogenic infections (9.79%). In 17.14% of patients there was no obvious cause. Tetanus following burns, post partum infection, boils and trauma had a high mortality (it was 100%, 50%, 50% & 44% respectively).

11. Tetanus neonatorum carries the highest mortality (82.92%).

12. In tetanus neonatorum the lesser the patients age, the more were the chances of mortality. Most neonatal deaths occurred between 4 to 11 days of age on admission and most recoveries beyond 11 days of age on admission.

13. Mustard oil and ash were the commonly used applications on the umbilical cord (30.49% & 9.7% of cases respectively).

14. All neonates were delivered mostly by untrained dais or elderly lady at home and unsterile shaving blade was the commonest instrument used for cutting the umbilical cord (89.02% of cases) in neonates.

15. In adults the shorter the duration of symptoms were before admission, the worse was the prognosis. Where the duration was beyond 7 days, prognosis was the best.

16. Lock jaw, neck rigidity, dysphagia and convulsions were the usual presenting features in adults & children. Inability to suck and excessive crying were the usual features in neonates.

17. Tetanus mortality increased with increasing grades of severity of tetanus. In grade I tetanus mortality was zero and in grade V 86.20%.

18. The shorter the incubation period, the worse was the prognosis of tetanus patients. (70.43% mortality was present with incubation period of less than 7 days, & with more than 21 days incubation period, 12.5% mortality was observed).

19. A shorter period of onset was associated with a worse prognosis. Where the period of onset was absent, mortality was the lowest (8.33%) and where it was less than 24 hours mortality was the highest (76.47%).

20. Higher mortality was observed in tetanus patients with raised temperature (99°F or above on admission or within 24 hours of admission).

21. Tetanus mortality increased with increasing severity of risus sardonicus.

22. Increased mortality was found in tetanus patients with increasing severity of neck rigidity.

23. Mortality in tetanus patients was proportional to the severity of dysphagia on admission. Increasing dysphagia was associated with worse prognosis (86.60% mortality with severe dysphagia).

24. Increased mortality was observed with increasing severity of lock jaw in tetanus patients on admission.

25. Tetanus mortality was directly related to the severity of spasms on admission. Without spasms the mortality was 6.66% whereas with severe spasms it was 80.99%.

26. T.I.G. was only effective when it was given as early as possible on admission. It was useless if administered on or beyond the IIIrd day of admission (mortality was 100%).

27. In tetanus therapy intrathecal administration of T.I.G. was more beneficial (mortality 45.32%) as compared to intramuscular T.I.G. (mortality 88.23%).

28. Intrathecal T.I.G. was more effective in all grades of severity of tetanus as compared to intramuscular T.I.G. in the same grades. Furthermore T.I.G. was most effective in milder cases of tetanus when used intrathecally (mortality 5.26%).

29. Higher doses of T.I.G. were more effective in lowering tetanus mortality. The mortality was 47.12% with a dose of 500 I.U. of T.I.G. Tetanus mortality was reduced to 38.46% with doses of 1000 I.U. Mortality fell to zero with doses of T.I.G. between 1500 I.U. and 3500 I.U. (only 7 patients were studied in this group as only they could afford it).
30. There was a higher incidence of tetanus in 1988 (285 cases) as compared to that in 1983 (178 cases). Mortality fell down from 68.53% in 1983 to 51.42% in 1988 with the use of intrathecal T.I.G. (in 1983 only A.T.S. was used).
31. Respiratory spasms leading to severe apnoea was the most important cause of death in tetanus. Pulmonary complications including acute secondary lung infections topped the list of complications in tetanus patients.

BIBLIOGRAPHY

B I B L I O G R A P H Y

1. Adams E B, Laurence D B and Smith J D W G: Tetanus. Blackwell Scientific publications, Oxford, 1964, P.31.
2. Athavale V B et al, J. Pediat., 1966, 68:289-93.
3. Ahmad Syah et al.: Comp. Study of procaine penicillin and metronidazole. Br.Med. T. (Clin. Res.), 7, 291, 1985.
4. Athavale V B et al.: "Tetanus neonatorum", edited by M.P.Anand, International symposium (1974), (Glaxo), Diptheria Pertussis Tetanus, 1975 Birkhauser Verlag Basel und Stuttgart.
5. Athavale, V B et al. : "Tetanus in childrem" edited by M.P. Anand, International symposium (1974), (Glaxo), Diptheria Pertussis Tetanus, 1975 Birkhauser Verlag Basel und Stuttgart.
6. Bytchenko, B. "Geegraphicsl distribution of tetanus in the world, 1951-60, a review of the problem", Bull'W.H.O. 34:71-104, 1966.
7. Box, G T.: " The treatment of tetanus " Pediatrics 1964, 32:872-7.
8. Bhandari N R. & Shrivastava V." A study of tetanus neonatorum: Different regimens of treatment", Indian Pediatrics 1980, 17:803-808.
9. Benjamin J. and Baltimore B.: J.A.M.A.: 1968(157) 205.

10. Bhat, A N and Anwikar, A K : Tetanus, A review of 888 cases, J Indian Med Assoc. 38:69, 1962.

11. Bhandari M R, et al.: " A study of tetanus neonatorum with special reference to effect of nerticosteroid therapy". Indian Pediatr 9: 607, 1973.

12. Bianchi (1961) Cited by Eckmann, L. Tetanus prophylaxis and therapy; p 2. New York, 1963.

13. Bhat G J, Mahrukh K, Joshi and Pravina W. Kandoth., " Neonatal tetanus - A clinical study of 100 cases", Indian Pediatr. Vol. 16, No. 2, p 159-165 (1979).

14. Bhandari B. et al.; "Intrathecal A.T.S. in management of tetanus neonatorum", Indian J. Med.Res. 1980; 72:685-7.

15. Bytchenko B D: Tetanus as a world problem, 'Principles on Tetanus', Proc. of the International conference on tetanus Berne, 15-19 July 1966 (Hans Haber Publishers. Bern and Stuttgart), p.21-41.

16. Bouyer Martin G. (Tetanus Neonatorum), Principles on tetanus P. 55(1966).

17. Blake P.A. et al: Serologic therapy of tetanus in United States 1965-1971.J.A.M.A. : 235:42, 1976.

18. Bhargava, S.: Tetanus neonatorum - A continuing problem. Editorial, Indian Pediatr., Vol. 17, No. 10: 785-786,1980.

19. Brown A. et al: Value of large dose of antitoxin in clinical tetanus. Lancet 2: 227, 1960.

20. Crandall D.L. et al : " Control of neuromuscular manifestations of severe systemic tetanus" J.A.M.A.: 1960 (15), 172.

21. Chugh K and Sehgal H.: " Evaluation of intrathecal human tetanus immunoglobulin in tetanus neonatorum" Indian Pediatric, Feb. 1985, 22-2; 153-8.

22. Chopra K., Gupta A. & Bhatre, K.:"Intrathecal tetanus hyperimmune human gamma globulin in the treatment of tetanus". Indian Pediatric Vol. 23, Oct. 1986; 775-778.

23. Cole L: " The prognosis of tetanus", Lancet, 1, 164, 1940.

24. Calvin K K, and Goldberg, Pregnosis in tetanus, J.A.M.A. 94; 1977 (1930).

25. Cole L. Youngman,: " Treatment of tetanus", Lancet 1: 197, 1969.

26. Edmonton R.S. & Flowers R.S.: Intensive care in tetanus management , complications and mortality in 100 cases". British Med.Jr. 1979; 1:1401-4.

27. Firor W M.: " Intrathecal administration of tetanus antitoxin" Arch. Surg. 41:299, 1940.

28. Forfar J O.: Neonatal tetanus in text book of Pediatrics, edited by J O Forfar and G C Ameil,Churchill Livingstone, London, 1973, p. 183-34.

29. Gupta P S., Kapoor R., Goyal S., Batra V.K. & Jain B.K. " Intrathecal Human Tetanus Immunoglobulin in early tetanus" Lancet,Aug., 30, 1980: 439-440.

30. Gordon, M.E., Singh, S. and Wyon J.B.: Tetanus in villages of Punjab, an epidemiologic study.J.I.M.A. 37:157, 1961.

31. Galazka, Arthur, M.: Control of neonat.tetanus. Ind. J. Paed., 52: 329-341, 1985.

32. Gupta P S, Kapoor R., : Int-rathecal use of human tetanus immunoglobulins. Clinician, 44, 127, 1980.

33. Gupta S. M. et al.: " A retrospective study of tetanus neonatorum and comparative assessment of diazepam in treatment. Indian Pediatr., 16, 543, 1979.

34. Haripasad D, Father M. Rocke D.A. & Wesley A.G.: " Renal function in tetanus" Intensive care medicine, 1984; 10:67-70.

35. Hendrickse R.G.and Sherman P.M.: "Tetanus in childhood a report of therapeutic trial of diazepam" British Medical Journal 1966; ii, 860-2.

36. Ildrim: "general and intrathecal serotherapy: Proceeding of the IV International conference on tetanus." Dakar 6:1975.

37. Ildrim I, et al.: Tetanus , New Eng J. Med.Vol. 280, No. 22, 1243.

38. Ildrim,: " Intrathecal serotherapy of tetanus", Turkish J. Paed., 16:103, 1974.

39. Jolly S.S. et al.: Tetanus in Punjab with particular reference to the role of muscle relaxants in its management". International symposium on Tetanus 1974, Diptheria

Pertussis Tetanus, edited by M.P. Anand (Glaxo), 1975, Birkheuser Verlag Basel und Stuttgart.

40.Japau K. et al.: Ascorbic acid in treatment of tetanus", Bengladesh Med. Res. Bull., 10(1): 24: Jun. 1984.

41.Kerr J.H.: Current topics in tetanus", Intensive care Medicine 1979; 5:105-10.

42.Kryzhanovsky G. N.:"Present data on pathogenesis of tetanus " Prog.Drug. Res. 1975; 19:301-13.

43.Kryzhanovsky G.N. & Krasnova N.M.: Intracisternal introduction of tetanus antitoxin in experimental tetanus intoxication, Bull Exp Biol Med. 71:38, 1971.

44.Keswani et al, Journal of the Indian Medical Association, Vol. 75, No. 4, 1980, 67-69.

45.Khanna S.S. et al.: " Neonatal tetanus : Psychomotor development in Survivors ", Indian Pediatric Vol. 22, No. 2, 1985, 125-130.

46.Kryzhanovsky G.N.: Tetanus: general and pathophysiological aspects;achievement,failures, Perspectives of Elaboration of the problem" Edited by M.P.Anand, Glaxo India Symposium, 1974, Diphheria Pertussis Tetanus, 138-145.

47.La Force et al, : Tetanus in United States (1965-1966), epidemiological and clinical features", New England J. Med. 280:569-574, 1969.

48.Laha P.N. and Vaishya V.D., J.I.M.A. 44, 422-36,1965.

49.Lall,J.C.,:" Indian Pediatrics, 16(8):693-5, Aug,1979.

50.Miller, J.K.: " The prevention of neonatal tetanus by maternal immunisation", Journal of Tropical Pediatrics and environmental child health, 18:160-167 (1972).

51.Maclennan, R. et al, : " Immunisation against neonatal tetanus in New guinea", Bull W.H.O.; 32:683-697, (1965).

52.Mac Walter, R.S., McFadden J.P. & Griffiths R.A.: "Tetanus presenting as hypothermia"Journal of the royal society of Medicine, Vol. 79, Oct 1986: 616-617.

53.Mathur, G.P., Singh Y.D., Sarla Mathur, Shared Chandra, : "Tetanus Neonatorum its epidemiology and management, " IndianPediatr, Vol. 17:10, 797-800, 1980.

54.Nyquist et al., Archives of Phys. Med. 39, 683 (1958).

55.Newell, K.W.: Tetanus Neonatorum, Epidemiology and Prevention, Principles on Tetanus P. 261-271.

56.Nkrumah, F.K., et al, " Neonatal tetanus", Ghana Med. J., 1971; 10:280-2.

57.Nkrumah F.K. & Neequaye J., " Failure of intrathecal A.T.S. to improve survival in neonatal tetanus", Archives of diseases of childhood, 1983, 58, 276-278.

58.Percy,A.S. et al.: " The continuing problem of tetanus S.G.O. Vol. 160,Apr 1985, No. 4,307-12.

59.Patel J.C., Joag G.G., : " Grading of tetanus to evaluate prognosis " Indian J Med Sc. 1959:13:834-840.

60.Patel J.C., Mehta B.C., Dhirwani M.K. and Trivedi R.R.: Tetanus Neonatorum, Indian J Child Health. 9:469,1960.

61.Phatak, A.T. & Shah S.B.: " Indices of Severity of Neonatal Tetanus ", Indian Pediatr.Vol. 10, No.2, P. 87-89, (1973).

62.Pascale L.R. et al, : " Treatment of tetanus by hyperbaric oxygenation", J.A.M.A.Vol.189, No.6,P. 408-410.

63.Phatak A.T. and Shah S.B.: " Tetanus Neonatorum", Ind. Paed. Clin. Ind, 5:115, 1968.

64.Sharma P.D. et al,: " Impact of alternate immunisation strategies on Tetanus Neonatorum in India", Indian Paediatr, Vol 21,No. 11, 1984, P. 839-849.

65.Spaeth, R.: Therapy of tetanus, a study of 276 cases, Arch Int. Med. 68: 1133, 1941.

66.Suri J.C.: The problem of Tetanus in India.Principles on tetanus, p 61-67.

67.Srivastava S.P. and G.G. Chatterji, J.I.M.A. 38, 71 (1962), Smith, W.H.,Br.Med.J. 1, 1090 (1953).

68.Sainani G.S. et al: " The status of Beta Adrenergic Blocking drug Propranolol in Severe Tetanus", J.Ass. Phys. Ind. 10, 789(1972).

69.Sanders R.K.M. et al: " Tetanus : Situational Clinical Trials and Therapeutics", Edited by M.P. Anand, International symposium on Tetanus (Glaxo) (1974), Diptheria Pertussis Tetanus, 1975 Birkhauser Verlag Basel und Stuttgart.

70.Smith, J.W.G.: " Tetanus and its Prevention" (guest lecture), edited by M.P. Anand, International symposium on Tetanus (Glaxo) 1974, Diptheria Pertussis Tetanus, 1975 Birkhauser Verlag Basel und Stuttgart.

71.Singh A.K. et al,: " Intrathecal ATS with steroids in treatment of neonatal tetanus", Arch Dis. Child, 55:527, 1980.

72.Sakhey J. & Bhargava I., " Control of neonatal tetanus in India", Indian Pediatrics, Vol. 21, 1984, P.515-519.

73.Sokal, D.C. et al,: " Mortality from neonatal tetanus in rural Cote d' Ivoire", Bull W.H.O. 66(1), 69-76 (1988).

74.Schofield,F.D. et al, British Medical Journal, 2:785-789 (1961).

75.Stanfield J.P. and Galazka A, " Neonatal tetanus in the world today", Bull' W.H.O. 62(4):647-669 (1984).

76.Sanders R.K.M., Joseph R., Martyn B., & Peacock M.L.,: "Intrathecal Antitetanus Serum (Horse) in the treatment of tetanus" Lancet, May 7, 1977, 1:974-7.

77.Smith et al,: " Treatment of tetanus neonatorum with I.P.P.V. " Lancet 1956 (2), 550.

78.Sherrington S.C.: " Observations with antitetanus serum in monkeys", Lancet 1917, ii:964-66.

79.Spaeth R: A clinical study of tetanus. Am.J. Dis. Child 60:130, 1940.

80.Shah, P.M. and Udani P.M.: Analysis of the vital statistics from rural community, Palghar II.

81.Sehgal, H., Wadhwa, S. and Lal, C.: "Evaluation of diazepam as an anticonvulsant in the treatment of tetanus neonatorum", Indian Pediatr, Vol. 15, No.2, P. 161-165.

82.Verma Y.S. et al,: " Semiprone position and continuous intragastric drip in conservative treatment of tetanus neonatorum", Ind.J.Paed., 47:388, Sept., 1980.

83.Venkat Raman G. and Lee H.A., " Tetanus and Renal failure ". British Journal of Clinical Practice July/August 1984, 38(7-8), 275-7.

84.Vakil B.J. et al, " Therapeutic trial of intracisternal human tetanus immunoglobulin in clinical tetanus," Trans R.Soc. Trop-Med.Hyg., 1979; 73:579-83.

85.Vaishnava,H., Goyal R.K., Neogy, C.N. & Mathur G.P.,: " A controlled trial of antiserum in the treatment of tetanus", Lancet, December, 1966, P. 1371-1373.

86.Vakil B.J. et al: "Cephalic Tetanus" edited by N.P. Anand, International symposium on Tetanus (Glaxo),1974.

Diptheria Pertussis Tetanus, 1975 Birkhauser Verlag Basel and Stuttgart.

87. Wesley A.G. & Pather M.: " Tetanus in children, an 11 year review" Annals of tropical pediatrics, 1987, 7, 32-37.